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(11)

EP 0 702 082 A1

EUROPEAN PATENT APPLICATION

(43) Date of publication:
20.03.1996 Bulletin 1996/12

(51) Int. Cl.⁶: C12N 15/13, C07K 16/42

(43) Application number: 94115683.8

(22) Date of filing: 05.10.1994

(84) Designated Contracting States:
AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL
PT SE

(30) Priority: 06.10.1993 JP 272950/93

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(54) **Amino acid sequences of anti-idiotypic antibodies against anti-cancer human monoclonal antibody, and dna base sequences encoding those sequences**

(57) Amino acid sequences of the H chain and L chain variable regions of mouse monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 against idio-types of a cancer cell antigen-specific human immunoglobulin CLN/IgG produced by a human/human fused cell strain CLN/SUZ H11, and base sequences of the genes of the variable regions are disclosed.

The above amino acid sequences and the base sequences are useful in medical and pharmaceutical fields such as prophylaxis, treatment and/or diagnosis of human diseases, and/or in pharmacological and/or biochemical fields, etc. such as biochemical reagents, and reagents for purification of biomacromolecules.

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Description

Detailed Description of the Invention

5 This invention relates to the structure of the variable regions of mouse immunoglobulins against idiotypes of an antigen-specific human immunoglobulin, useful in wide fields, for example in pharmaceutical fields such as prophylaxis, treatment and/or diagnosis of human diseases, and/or in pharmacological and/or biochemical fields such as biochemical reagents and reagents for purification of biomacromolecules.

10 More detailedly, this invention relates to the amino acid sequences of the H chain and L chain variable regions of mouse immunoglobulins against idiotypes of a cancer cell antigen-specific human immunoglobulin produced by a human/human fused cell strain CLN/SUZ H11 from a B cell of a patient carrying human cervical carcinoma and a human lymphoblastoid cell strain, and relates to the base sequences of the genes of the variable regions.

15 Since the development of the technique of formation of monoclonal antibodies by cell fusion or immortalization of cells, many useful antibodies have been obtained using mainly mice. Among them, monoclonal antibodies against malignant tumor cells are utilized not only for fundamental researches such as analyses of tumor antigens, but in serum diagnoses, image diagnoses of tumors using labeled antibodies, and have extremely high utilization value. Particularly, human-derived anti-cancer monoclonal antibodies are expected as ideal antibodies in the clinical field, since they have only faint or no side effects.

20 In such circumstances, one of the present inventors, as disclosed detailedly in Japanese Laid-Open Patent Publication No. 201994/1983 (= U. S. Patent No. 5,286,647; EP-A-839,02157.3), Japanese Laid-Open Patent Publication No. 135898/1984 and Japanese Laid-Open Patent Publication No. 137497/1984, established a cell strain CLN/SUS H11 (ATCC No. HB 8307) which produces a human monoclonal antibody having a high reactivity with human cancer cells. Interesting findings are obtained about the antibody (named CLN-IgG) produced by this cell strain, that the antibody class is IgG; the isotypes are $\gamma 1$ type and κ type; and the antibody binds to a cancer antigen immunohistologically existing on the surface of the cancer cells and moreover inhibits proliferation of the cancer cells. At present, the whole amino acid sequence and DNA base sequence of the antibody are clarified (Japanese Laid-Open Patent Publication No. 346792/1992 = WO 92/20799).

30 On the other hand, since Jerne put forward the so-called network theory, various researches have been made on the structure of the variable regions of antibodies. An antibody binds to an antigen at its variable region (antigen combining site). Therefore, the variable regions of antibodies have various three-dimensional-like structures in accordance with the structures of the antigenic determinants on the surfaces of antigens to be recognized. Thus, an antibody itself can be considered to be an antigen, and in the case, the structures of the variable regions of the antibody are called idiotypes, and antibodies against the idiotypes of the antibody are called anti-idiotypic antibodies. The structure corresponding to an antigenic determinant is called an idiope. An idiope can be thought to be an aggregate of idiotypes. It was reported 35 that among anti-idiotypic antibodies (Ab2) against an antibody (Ab1) exist antibodies which competitively inhibit binding of Ab1 to an antigen and have idiopes analogous to antigens recognized by the antibodies, i.e. antibodies having structures as so-called internal images of the antigen.

In view of the above findings, anti-idiotypic antibodies are expected to be utilized for the purpose of treatment and/or diagnosis of cancers.

40 For example, as for the purpose of cancer treatment, a vaccine therapy using an anti-idiotypic antibody as an antigen is made possible. It is generally difficult to get cancer antigens in large amounts, and it is restricted from a safety aspect and an ethical aspect to directly immunize human beings with cancer cells as antigens. Therefore, these problems can be avoided by performing immunization with an anti-idiotypic antibody in place of an antigen.

45 In a diagnostic aspect, anti-idiotypic antibodies can be utilized to examine the state of immune reactions against cancer cells. Specifically, it serves for early detection of cancers, judgment of therapeutic effects to detect or determine one's antibodies against cancer antigens existing in the blood or humor of cancer patients.

Under such technical background, problems as stated below are underlying to be solved.

50 1) When anti-idiotypic antibodies are utilized as vaccines or diagnostic drugs, it is necessary to provide these antibodies in large amounts and stably. 2) There is a possibility to give more powerful vaccines or diagnostic drugs abounding in functionality by altering or modifying the antibodies.

A method by gene manipulation is considered as a means for solving the above problems, i.e. a means for realizing improvement of production amount of the antibodies and elevation or modification of the activities of the antibodies.

60 For example, in the case of the problem of 1), it can be considered to solve the problem by cloning such an antibody gene, introducing the gene into host cells such as animal cells or *Escherichia coli*, expressing the antibody gene to give a large amount of the antibody, and in the case of the problem of 2), it can be considered to alter such an antibody so as to have stronger immunogenicity by artificially changing the antibody gene, or to design an antibody molecule having a higher vaccinal activity by adding a function which the antibody does not inherently have, for example an enzymatic activity, an immunity induction activity or the like to the antibody molecule or a fragment thereof.

For accomplishment of these purposes, separation of anti-idiotypic antibody genes, and clarification of their structures are necessary. However, there has not so far been known anything at all about the structures of L chains and H chains constituting anti-idiotypic antibodies against idiotypes of CLN-IgG, and the gene structures of the variable regions having a function to specifically bind to idiotopes of CLN-IgG.

5 Thus the main object of this invention is to clarify the gene structures of the L chains and the H chains of anti-CLN-IgG idiotype antibodies.

The present inventors have succeeded in creating hybridomas producing, respectively, five kinds of mouse anti-CLN-IgG idiotype antibodies (Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33) having $\gamma 1$ and κ isotypes against the idiotypes of CLN-IgG; have separated, from the hybridomas, cDNAs encoding the L chains and H chains of the anti-idiotypic
10 antibodies, respectively; have clarified their DNA base sequences; have determined, based on these sequences, the amino acid sequences of the L chains and H chains of the antibodies, respectively; and have completed this invention.

Thus, according to this invention are provided an immunoglobulin H chain variable region fragment which contains a hypervariable region CDR1 having an amino acid sequence selected from

15

(1) Ser Tyr Trp Met His;
Asp Tyr Tyr Met Asn; and
Asn Tyr Trp Met Gln,

20

a hypervariable region CDR2 having an amino acid sequence selected from

25

(2) Ala Ile Tyr Pro Gly Asn Ser
Asp Ile Ser Tyr Ser Gln Asn
Phe Lys Asp;
Phe Ile Arg Asn Lys Ala
30 Asn Leu Tyr Thr Thr Asp
Tyr Ser Ala Ser Val Lys
Gly;
Phe Ile Arg Asn Lys Ala
35 Asn Tyr Tyr Thr Thr Glu
Tyr Ser Ala Ser Val Lys
Gly; and
40 Ala Ile Tyr Pro Gly Asp
Gly Asp Thr Arg Tyr Thr
Glu Lys Phe Lys Gly ,

45

50

55

and a hypervariable region CDR3 having an amino acid sequence selected from

(3) Glu Glu Tyr Asp Tyr Asp
 Thr Leu Asp Tyr;
 Asp Arg Gly Gly Arg Asp
 Trp Tyr Phe Asp Val;
 Asp Gly Phe Leu Arg Asp
 Trp Tyr Phe Asp Val; and
 Ser Gly Tyr Tyr Gly Ser
 Phe Val Gly Phe Ala Tyr ;

and DNA and RNA fragments encoding the immunoglobulin H chain variable region fragment.

According to this invention are further provided an immunoglobulin L chain fragment which contains a hypervariable region CDR1 having an amino acid sequence selected from

(1) Tyr Arg Ala Ser Lys Ser Val
 Gln Leu His Leu Ala Ile Val
 Tyr Met His;
 Tyr Arg Ala Ser Lys Ser Val
 Ser Thr Ser Gly Tyr Ser Tyr
 Met His;
 Lys Ala Ser Gln Asp Val Asn
 Thr Ala Val Ala; and
 Lys Ala Ser Gln Asp Val Thr
 Thr Asp Val Ala ,

a hypervariable region CDR2 having an amino acid sequence selected from

(2) Leu Val Ser Asn Leu Glu Ser;
 Leu Val Ser Asn Leu Asp Ser; and
 Ser Ala Ser Tyr Arg Tyr Thr ,

and a hypervariable region CDR3 having an amino acid sequence selected from

- (3) Gln His Ile Arg Val Ala Tyr
 5 Thr;
 Gln His Ile Arg Gly Ala Tyr
 Thr;
 10 Gln His Ile Glu Gly Ala Tyr
 Thr;
 Gln Gln His Tyr Ser Pro Pro
 Leu Thr; and
 15 Gln Gln His Tyr Ser Thr Ala
 Trp Thr;

20 and DNA and RNA fragments encoding the immunoglobulin L chain variable region fragment.

In this invention, cytoplasmic RNAs were prepared from the five mouse hybridomas, respectively; the RNAs were converted to cDNAs by a reverse transcriptase; the antibody genes were amplified using these cDNAs as templates and using the PCR method; the amplified DNA fragments were integrated into plasmids and cloned; the base sequences of the insertion DNAs of the plasmids purified from *Escherichia coli* clones isolated were determined, and the amino acid sequences were determined based on the base sequences. These steps are further detailedly described below.

[1] Isolation of cytoplasmic RNAs

Each mouse hybridoma is cultured and proliferated in a culture medium, e.g. and RDF or RPMI 1640 medium, containing 5% fetal bovine serum under a suitable condition, e.g. under a condition of 37°C and a carbon dioxide concentration of 5%; the resultant cells are collected by centrifugation; and the cytoplasmic RNA is extracted from the cells by a conventional method, e.g. a method disclosed in 7.12 of Molecular Cloning (2nd edition, edited by Sambrook et al., Cold Spring Harbor Laboratory Press 1989). The resultant cytoplasmic RNA can further be utilized as a template for cDNA synthesis. Specifically in this invention, the cytoplasmic RNAs were extracted from mouse hybridomas No. 3, No. 17, No. 20, No. 27 and No. 33, and provided for synthesis of cDNAs.

[2] Synthesis of cDNAs

Using a cytoplasmic RNA obtained in the step of [1] as a template, a single-strand DNA complementary to the mRNA is synthesized in the presence of dATP, dGTP, dTTP and dCTP using, as a primer, an oligo dT corresponding to a poly A, or a synthetic nucleotide having a random sequence, and a reverse transcriptase. In the specific operations in the invention, cDNAs were synthesized using the cytoplasmic RNAs obtained in the step of [1] as templates and a random hexamer as a primer, respectively, and provided for the step of amplification of the antibody genes.

45 [3] Amplification of antibody genes by PCR

PCR reaction is performed in the presence of dATP, dGTP, dTTP, dCTP and Taq polymerase using as a template a single-strand cDNA obtained in the step of [2] and as a primer a sequence of the antibody gene (e.g., a sequence encoding a constant region, a variable region or a leader region of the antibody gene) to amplify the antibody gene. Suitably in the invention, the antibody genes were amplified using as templates the single-strand cDNAs obtained in the step of [2] and using synthetic DNA oligomers corresponding to the sequences of the leader regions and variable regions of the L chains and H chains of the antibodies, respectively.

[4] Cloning of PCR-amplified DNA fragments

55 A PCR-amplified DNA fragment obtained in the step of [3] is, directly or after treatment with restriction enzyme(s), ligated into one of various vectors, for example plasmid vectors such as pUC 18, pCR1000 and pCR™, phage vectors such as M 13 phage, and phagemid vectors such as pUC 118 and pBluescript SK+ to prepare a vector containing the insertion fragment. Then, *Escherichia coli* is transformed with the vector, and a colony of the *Escherichia coli* containing

the targeted antibody gene fragment is obtained. The purified vector recovered from the *Escherichia coli* is provided as a sample for determination of the DNA base sequence. In the specific operations in the invention, the PCR-amplified DNA fragments obtained in the step of [3] were directly ligated, respectively, into pCR1000 and pCR™ plasmid vector; an *Escherichia coli* INVαF was transformed with each of the resultant plasmids; and the plasmids were purified from the resultant *Escherichia coli* colonies, respectively.

[5] Determination of the base sequences and amino acid sequences of the DNAs

The base sequence of the DNA at the insertion site in a plasmid obtained in the step of [4] can be determined using the Maxam-Gilbert method or the Sanger method. In the invention, the pCR1000 or pCR™ plasmid vectors containing the insertion fragments were purified, respectively; their base sequences were determined by the Sanger method; and the amino acid sequences were presumed based on their base sequences, respectively.

Hereafter, this invention is further specifically described below according to examples.

Drawings referred to in Examples are briefly described as follows.

Fig. 1 is a drawing showing isotypes of monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33.

Fig. 2 is a drawing showing the monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 specifically bind to CLN-IgG, and do not bind to other human IgGs.

Fig. 3 is a drawing showing that monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 are competitively inhibiting the binding between CLN-IgG and human matricial carcinoma cell ME-180.

Fig. 4 is a drawing where the amino acid sequences of the H chain variable regions of monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 are notated in parallel according to the Kabat's notation, and the regions of the hypervariable regions CDR1, CDR2 and CDR3 are determined.

Fig. 5 is a drawing where the amino acid sequences of the L chain variable regions of monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 are notated in parallel according to the Kabat's notation, and the regions of the hypervariable regions CDR1, CDR2 and CDR3 are determined.

Example 1: Preparation of mouse hybridomas

100 µl of 1 mg/ml human IgG (produced by Cappel) is intraperitoneally injected to a Balb/c mouse on the first day after its birth to prepare a mouse having immunological tolerance to human IgG. Six weeks later, the mouse is immunized as follows with CLN-IgG as an antigen.

CLN-IgG purified from a culture medium of a human/human hybridoma CLN/SUZ H11 (ATCC No. HB8307) according to an ammonium sulfate precipitation method and protein A-affinity chromatography was adjusted to a concentration of 2 µg/µl with physiological saline; an equal amount of complete Freund's adjuvant solution was added; and after mixing and emulsification, 100 µl of the emulsion (corresponding to 100 µg of CLN-IgG) was subcutaneously injected into the immunologically tolerated mouse. Thereafter, similar immunization was repeated 4 to 5 times, the murine spleen was enucleated 4 days after the final immunization and made to be spleen cells, and they were used for the following cell fusion.

A mouse parent cells NS-1 (ATCC TIB 18) and the spleen cells are washed with portions of RPMI 1640 medium not containing serum, respectively, and the both of the cells are mixed and centrifuged. 1 ml of 50% polyethylene glycol (average molecular weight : 4,000) is added dropwise to the resultant precipitate over a period of 1 minute. 10 ml of RPMI 1640 medium is further added over a period of 3 minutes, the mixture is centrifuged at 400 x g for 5 minutes, the precipitate is suspended in 10 ml of RPMI 1640 medium containing 20% fetal bovine serum, and the suspension is spread into a 96-well microplate.

Thereafter, the cells were cultured in HAT medium for 14 to 21 days, transferred to HT medium, and finally cultured in RPMI 1640 medium containing 10% fetal bovine serum.

The antibody titers in the culture supernatants on the wells where proliferation was observed were assayed by an enzyme-labeled antibody technique; hybridoma clones secreting monoclonal antibodies which bind to CLN-IgG but not to human IgG were obtained from the appropriate wells by the limiting dilution method; and these hybridoma clones were named No. 3, No. 17, No. 20, No. 27 and No. 33.

Example 2: Determination of isotypes of the mouse antibodies

Isotypes of the antibodies secreted from the 5 mouse hybridomas obtained in Example 1 were determined as follows using a mouse monoclonal antibody isotyping kit (produced by Amersham Co.).

The mouse hybridomas are started to be cultured at a concentration each of 5×10^4 /ml in portions of RPMI 1640 medium containing 10% fetal bovine serum, respectively, and 5 days later the culture supernatants are obtained, one stick portions of the typing sticks are placed in test tubes, respectively; 3 ml portions of the culture supernatants 5-fold diluted with TBS-T (Tris-buffered saline (TBS, pH 7.6) containing 0.1% Tween 20) are added thereto respectively; and

the mixtures are incubated at room temperature for 15 minutes. The culture supernatants are discarded, 5 ml portions of TBS-T are added, and the typing sticks are washed at room temperature for 5 minutes. TBS-T was discarded, and the washing was repeated once more. 3 ml portions of a peroxidase-labeled anti-mouse antibody 500-fold diluted with TBS-T are added, and the mixtures are incubated at room temperature for 15 minutes. The typing sticks are washed twice in the same manner as above; 3 ml portions of an enzyme substrate solution (obtained by adding one drop of 30% aqueous hydrogen peroxide to 50 ml of a TBS solution of 4-chloro-1-naphthol) are added; the mixtures are subjected to reaction at room temperature for 15 minutes; and then the sticks are washed with distilled water. The isotypes of the mouse antibodies are determined based on the resultant signals, respectively.

As a result, as shown in Fig. 1, all the isotypes of these antibodies were $\gamma 1$ and κ .

Example 3: Examination of specificities of the anti-idiotypic antibodies

It was examined according to a dot blot technique, using an ECL Western blotting detecting reagent (produced by Amersham Co.), that the mouse anti-CLN-IgG idiotype antibodies specifically bind to CLN-IgG. The process is stated below.

CLN-IgG and human IgG1 (produced by Protogen Co.) were diluted with PBS to concentrations of 50 to 0.2 $\mu\text{l/ml}$, respectively. 2 μl portions of the thus prepared samples were spotted on a number of Hybond-ECL nitrocellulose membrane (produced by Amersham Co.), respectively and after being dried, the nitrocellulose membranes were allowed to stand at room temperature for one hour in PBS-T (0.3% Tween 20-containing PBS) containing 5% skim milk. After being washed with PBS-T, the nitrocellulose membranes were allowed to stand at room temperature for one hour in the culture supernatants (500-fold diluted with PBS-T) of mouse hybridomas No. 3, No. 17, No. 20, No. 27 and No. 33, respectively. After being washed with PBS-T, the nitrocellulose membranes were allowed to stand at room temperature for one hour in portions of a peroxidase-labeled sheep anti-mouse Ig antibody 3,000-fold diluted with PBS-T, respectively. After being washed with PBS-T, the nitrocellulose membranes were subjected to reaction for one minute in portions of the ECL detecting reagent, and sheets of X-ray film were exposed for 30 seconds to the light emitted from the resultant nitrocellulose membranes, respectively.

The results of the sheets of X-ray film developed are shown in Fig. 2. Any of the five antibodies bound to CLN-IgG, but did not bind to human IgG1. Namely, it was revealed that these antibodies are specific to CLN-IgG.

Next, it was examined whether or not the mouse antibodies have an activity to inhibit the binding of a human monoclonal antibody CLN-IgG to a human cancer cell. The method is stated below.

A human cervical carcinoma cell ME-180 (available from ATCC) is cultured in DF medium (a 1:1 mixed medium of DME : F-12) containing 10% fetal bovine serum. At the stage when the number of the cells becomes 5×10^6 to 1×10^7 , the cells are detached from the bottom face of the Petri dish using trypsin, collected by centrifugation and sufficiently washed with the medium. A constant number ($10^5/100 \mu\text{l}$) each of the cells is placed in each well of a 96-well microtiter plate, and allowed to stand at 37°C overnight to be attached on the plate. 50 μl portions of 3% glutaraldehyde solution were added dropwise into the respective wells, and the mixtures are allowed to stand at 37°C for 20 minutes to fix the cells. The cells of each well are centrifuged at $200 \times g$ for 10 minutes and washed three times with a gelatin buffer (10 mM phosphate-buffered physiological saline containing 0.3% gelatin); 200 μl portions of 1% bovine serum albumin (BSA) solution are added dropwise; and the mixture is allowed to stand at 37°C for one hour to block the plate. The cells are washed three times with the gelatin buffer to remove BSA not adsorbed. Thereafter, dilutions at various rates (100 to 1,000,000-fold) of the ascites obtained by intraperitoneally inoculating into mice the various hybridomas secreting the mouse anti-idiotypic antibodies are added dropwise together with CLN-IgG (50 μg each), and the mixtures are subjected to reaction at 37°C for one hour. The cells of these wells are washed three times with the gelatin buffer, 50 μl portions of a 3,000-fold diluted peroxidase-conjugated goat anti-human Ig antibody (produced by TACO Co.) are added dropwise, respectively, and the mixtures are subjected to reaction at 37°C for 30 minutes. The cells are washed three times with the gelatin buffer, and portions of a substrate solution containing hydrogen peroxide and o-phenylenediamine are added to perform reaction in a darkroom. 10 minutes later, 50 μl portions of 5N sulfuric acid are added to stop the reaction. When the peroxidase-conjugated goat anti-Ig antibody remains on the microplate, namely when the human IgG to be bound thereto remains, a yellow reaction product having absorption at 490 nm is formed. The amount of CLN-IgG bound to the cancer cell is determined by measuring the amount of the reaction product by a spectrometer.

It was clarified, according to the above method, that all the mouse antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 inhibit the binding of CLN-IgG to the cancer cell (Fig. 3).

From the foregoing, these mouse antibodies are antibodies against the idiotypes of CLN-IgG.

Example 4: Preparation of RNA

From the five kinds of mouse hybridomas No. 3, No. 17, No. 20, No. 27 and No. 33, the cytoplasmic RNAs were extracted according to the method disclosed in Molecular Cloning (2nd edition, edited by Sambrook et al., Cold Spring Harbor Laboratory Press 1989) 7, 12, as stated below.

10⁸ each of the hybridomas cells are collected by centrifugation, and washed twice with 10 times each precipitate's volume of a phosphate-buffered saline. The cells of these groups are centrifuged at 2,000 x g and 4°C for 5 minutes, and the resultant precipitates are suspended in 200 µl portions of an RNA extracting solution (0.14 M NaCl, 1.5 mM MgCl₂, 10 mM Tris-HCl pH 8.6, 0.5% Nonidet P-40, 1 mM dithiothreitol, 20 mM vanadylribonucleoside complex), respectively. The suspensions are subjected to vortex for 15 seconds and allowed to stand on ice for 5 minutes. The resultant suspensions are centrifuged at 12,000 x g for 30 seconds to remove the cell nuclei as precipitates; to the supernatants are, respectively, added 200 µl portions of a proteinase buffer (0.2 M Tris-HCl pH 8.0, 25 mM EDTA pH 8.0, 0.3 M NaCl, 1.2% SDS) and 1 µl portions of an aqueous proteinase K solution (20 mg/ml); and the mixtures are sufficiently stirred and subjected to incubation at 37°C for 30 minutes. Equal volume portions of phenol/chloroform are added to the reaction solutions, respectively, and the mixtures are stirred, centrifuged at 5,000 x g and room temperature for 10 minutes, and then allowed to separate into organic layers and aqueous layers, respectively. 400 µl portions of isopropanol cooled on ice in advance are added to the aqueous layers recovered, respectively, and the mixtures are allowed to stand on ice for 30 minutes. The mixtures are centrifuged at 12,000 x g and 4°C for 10 minutes to collect RNAs. The resultant RNA precipitates are washed with 1 ml portions of ethanol, dried under reduced pressure and suspended in appropriate amount portions of TE buffer, respectively. Using the cytoplasmic RNAs obtained according to the above operations, the antibody genes are amplified.

Example 5: Amplification and cloning of the antibody genes by the RT-PCR method

The antibody genes were amplified from the cytoplasmic RNAs obtained in Example 4, using a GeneAmp® RNA PCR kit (produced by Takara Shuzo Co., Ltd.). First, 20 µl each of reactive solutions were prepared containing PCR buffer II (x1), 5 mM MgCl₂, 1 mM dATP, 1 mM dGTP, 1 mM dTTP and 1 mM dCTP, 1 U/µl an RNase inhibitor, 2.5 µM a random hexamer, 2.5 U/µl a reverse transcriptase and 100 ng each of the above-mentioned cytoplasmic RNAs, respectively; 20 µl portions of a mineral oil were overlaid thereon respectively; and incubations were performed at room temperature for 10 minutes, at 42°C for 15 minutes, at 99°C for 5 minutes and then at 4°C for 5 minutes to perform cDNA synthesis by reverse transcription reaction. Then, 80 µl portions of a solution consisting of 4 µl of 25 mM MgCl₂, 8 µl of 10x PCR buffer II, 65.5 µl of sterile distilled water, 0.5 µl of AmpliTaq DNA polymerase (5 U/µl) and 2 µl of PCR primers (each 100 pmoles) were added to the above 20 µl of the reverse transcription reaction solutions; 80 µl portions of the mineral oil were overlaid thereon; and PCR reactions were successfully performed. Each reaction was performed by repeating 30 times the cycle of 94°C for 1.5 minutes, 50°C for 2 minutes and then 72°C for 3 minutes. The base sequences of the PCR primers are shown below. The primers contained in a Ig-Prime™ kit (produced by Novagen Co.) were used except for the primer of the leader sequence C for H chains.

Primer for H chains	
Leader sequence A	5' GGGAATTCATGRASTTSKGGYTMARCTKGRTTT 3'
Leader sequence B	5' GGGAATTCATGRAATGSASCTGGGYWTYCTCTT 3'
Leader sequence C	5' TTAAATGGTATCCAGTGT 3'
Constant region	5' CCCAAGCTTCCAGGGRCCARKGGATARACIGRTGG 3'

Primer for L chains	
Leader sequence A	5' GGGAATTCATGRAGWCACAKWCYCAGGTCTTT 3'
Leader sequence B	5' GGGAATTCATGGAGACAGACACACTCCTGCTAT 3'
Constant region	5' CCCAAGCTTACTGGATGGTGGGAAGATGGA 3'

In the above, the alphabets other than A, G, C and T mean the following bases. R=A/G, W=A/T, I=inosine, Y=C/T, D=A/G/T, K=G/T, H=A/C/T, S=C/G, V=A/C/G, M=A/C, B=G/C/T

10 µl portions of the resultant 100 µl each of the PCR reaction products are subjected to 1.5% agarose gel electrophoresis, and it was confirmed that the antibody gene fragments each about 600 bp long were amplified. As a result, in the case of the H chains, the antibody genes derived from No. 3 and No. 17 were amplified in the leader sequence A,

the antibody genes derived from No. 20 and No. 27 were amplified in the leader sequence B, and the antibody gene derived from No. 33 was amplified in the leader sequence C. On the other hand, in the L chains, the antibody genes derived from No. 27 and No. 33 were amplified in the case where the leader sequence A was used, and the antibody genes derived from No. 3, No. 17 and No. 20 were amplified in the leader sequence B.

5 Each of the PCR-amplified fragments about 600 bp long was integrated into pCR 1000 vector or pCR™ vector using TA cloning kit (produced by Invitrogen Co.). Specifically, ligation mix solutions were prepared by mixing 1 µl portions of the PCR reaction products, 1 µl portions of 10 x the ligation buffer, 2 µl portions of pCR1000 or pCR™ vector (corresponding to 50 µg), 1 µl of T4 DNA ligase and 6 µl portions of sterilized water, respectively; and incubated overnight at 12°C. Separately, 50 µl portions of a suspension of a competent *Escherichia coli* INVαT strain, to which portions were
10 added 2 µl portions of 0.5 M β-mercaptoethanol, respectively, were prepared; and 1 µl portions of the above ligation mix solutions are added thereto, respectively. The mixtures are allowed to stand on ice for 30 minutes, incubated at 42°C for one minute, and rapidly cooled on ice for 2 minutes. 450 µl portions of SOC medium warmed to 42°C in advance were added to the resultant *Escherichia coli* solutions, respectively, and the mixtures are cultured with shaking at 37°C for one hour. Meanwhile, 25 µl portions of X-Gal (40 mg/µl) are spreaded onto a number of LB agar plates each containing
15 Kanamycin (50 µg/ml), respectively, and the agar plates are incubated at 37°C until each X-Gal completely permeates the agar plate.

200 µl portions of the *Escherichia coli* culture broths after completion of culture were spread on the agar plate dried, respectively, and the plates were allowed to stand at 37°C overnight to give white colonies each having Kanamycin resistance.

20 Plasmids were purified from the *Escherichia coli* clones containing the respective antibody genes, and named 3KB11, 17KB1, 20KB1, 27KA2, 33KA26, 3GB1, 17GB7, 20GA2, 27GA5 and 33GC003, respectively. Purification of the plasmids is performed as follows.

The *Escherichia coli* strains containing the above plasmids, respectively, are cultured 37°C overnight in 100 ml portions of LB medium containing Kanamycin (50 µg/ml), respectively. Each of the resultant culture broths is centrifuged
25 at 3,000 rpm for 10 minutes; the cells collected are suspended in 3 ml of an ice-cooled suspension (50 mM glucose, 10 mM EDTA, 2 mM Tris-HCl pH 8.0); and the suspension is allowed to stand at room temperature for 5 minutes. 6 ml of an alkali lysing solution (0.2 N sodium hydroxide, 1% SDS) is added, and the mixture is mixed by gently turning the centrifugation vessel upside down, and allowed to stand on ice for 5 minutes. 4.5 ml of an ice-cooled neutralizing solution (5 M potassium acetate pH 4.8) is added, and the mixture is centrifuged at 12,000 rpm and 4°C for 10 minutes. The
30 supernatant is transferred into another centrifugation vessel; 1 ml of heat-treated 100 µg/ml RNase A solution is added; and the mixture is subjected to reaction for one hour in an incubator of 37°C to perform RNA digestion. To the reaction solution are added 6 ml of TE buffer-saturated phenol and 6 ml of chloroform/isoamyl alcohol (24:1), and the mixture is subjected to vortex for 30 seconds and then centrifuged at 10,000 rpm and 4°C for 3 minutes. The aqueous layer is transferred into another centrifugation vessel, an equal amount of isopropanol is added, and the mixture is sufficiently
35 mixed and then centrifuged at 10,000 rpm and room temperature for 10 minutes.

The resultant precipitate is washed with 1 ml of 70% cold (-20°C) ethanol, dried under reduced pressure, and dissolved in 480 µl of sterilized water. The solution is transferred into an Eppendorf tube; 120 µl of 4 M NaCl and 600 µl of 13% polyethylene glycol #6000 are added; and the mixture is allowed to stand on ice for 20 minutes. The mixture is then centrifuged at 10,000 rpm and 4°C for 10 minutes, and the precipitate is washed with 1 ml of 70% cold (-20°C) ethanol,
40 dried under reduced pressure and dissolved in 100 µl of TE buffer. The resultant purified plasmid was used as a template for sequencing reaction.

Example 6: Determination of the base sequences

45 Sanger reactions were performed using as templates the plasmids cloning purified in Example 5 and a fluorescence-labeled primer; the reaction products were analyzed by a DNA sequencer DSQ-1 (produced by Shimadzu Corporation); and the DNA base sequences of the insert parts of the plasmids were also determined.

The sequencing reactions were performed using AmpliTaq cycle sequencing kit (produced by Takara Shuzo Co., Ltd.) and a fluorescence-labeled primer in a reagent kit (produced by Wakunaga Pharmaceutical Co., Ltd.) exclusively
50 used for a fluorescence-type DNA sequencer. First, 2 to 4 µg of one of the plasmids purified as stated in Example 5 is mixed with 1 µl of the FITC-labeled primer (1 p mole/µl, forward or reverse is used) and 2 µl of the 10 x cycling mix solution, and sterilized water is added to prepare 10 µl in final volume of a reaction mix. Four tubes are prepared in which 2 µl portions of the termination mix (A, G, C, T) were placed in advance, respectively. 2 µl portions of the above reaction mix were taken and placed into the respective tubes. The mixtures are corrected by centrifugation, 10 µl portions
55 of a mineral oil are overlaid, and cycling reactions are performed under the following conditions; Precycle 95°C, 3 minutes; first cycle 95°C 30 seconds, 60°C 30 seconds, 72°C 1 minute (repeated 15 times); second cycle 95°C 30 seconds, 72°C 1 minute (repeated 15 times); postcycle 4°C.

2 µl portions of a reaction-stopping dye solution (95% formaldehyde, 20 mM EDTA, 0.05% methyl violet) are added, and the mixtures are mixed by centrifugation and preserved at 20°C until they are electrophoresed.

As 5% polyacrylamide gel was used, one obtained by adding pure water to 30 g of urea, 6 ml of 10 x TBE buffer (0.89 M Tris-HCl, 0.89 M boric acid, 0.025 M EDTA disodium salt) and 10 ml of 30% acrylamide solution (28.5% acrylamide and 1.5% methylenebisacrylamide, both produced by BIO-RAD Co.) to make the whole volume 60 ml; filtering the mixture with 0.22- μ m filter; deaerating the filtrate for 30 minutes; adding 150 μ l of 10% ammonium persulfate and 15 μ l of TEMEO; allowing the mixture to stand overnight to make it gel.

The gel was set in the DNA sequencer DSQ-1, and prerun was performed at a constant voltage of 1,000 V for one hour. Each of the samples was denatured at 95°C for 3 minutes immediately before electrophoresis, and rapidly cooled on ice, and 2 to 3 μ l of the reaction solution was sucked up from the bottom part of the tube by a micro-syringe and loaded onto the gel. Samples run was performed at a constant electric power of 20 W for 12 hours.

After completion of electrophoresis, the base sequence was determined using the software attached to DSO-1. The sequence was confirmed by sequencing both of the sense and antisense chains of the same plasmid from both directions.

The resultant base sequences of the variable regions of the H chains and L chains of the five kinds of the mouse monoclonal antibodies, and amino acid sequences presumed therefrom are shown in the following sequence listing. Relation between the sequence numbers and the sequences of the clones are as follows:

- Sequence No. 1 : Idio 3 H chain variable region (clone 3GB1)
- Sequence No. 2 : Idio 17 H chain variable region (clone 17GB7)
- Sequence No. 3 : Idio 20 H chain variable region (clone 20GA2)
- Sequence No. 4 : Idio 27 H chain variable region (clone 27GA5)
- Sequence No. 5 : Idio 33 H chain variable region (clone 33GC003)
- Sequence No. 6 : Idio 3 L chain variable region (clone 3KB11)
- Sequence No. 7 : Idio 17 L chain variable region (clone 17KB1)
- Sequence No. 8 : Idio 20 L chain variable region (clone 20KB1)
- Sequence No. 9 : Idio 27 L chain variable region (clone 27KA2)
- Sequence No. 10 : Idio 33 L chain variable region (clone 33KA26)

Example 7 Determination of hypervariable regions

The amino acid sequences obtained in Example 6 were notated in parallel according to the numbering of Kabat et al.'s data base (Sequences of proteins of immunological interest Fifth edition, U. S. Department of health and human services. Public health service, National Institutes of Health. NIH Publication No. 91-3242, Kabat et al. 1991), and the amino acid sequences of the hypervariable regions CDR1, CDR2 and CDR3 of each antibody were identified (Fig. 4, H chains, Fig. 5 L chains). In order to confirm the novelty of the identified amino acid sequences of the hypervariable regions CDR1, CDR2 and CDR3, retrieval by a computer was performed using the above Kabat et al.'s data base and a protein data base NBRF-PDB (National Biomedical Research Foundation - protein data base) Release 36.

As a result, the amino acid sequences of Idio 3 H chain CDR1, Idio 17 H chain CDR1, Idio 20 H chain CDR1, Idio 27 H chain CDR1, Idio 33 H chain CDR2, Idio 3 L chain CDR2, Idio 17 L chain CDR2, Idio 27 L chain CDR2 and Idio 33 L chain CDR2 were the same as those of known antibodies, but the amino acid sequences of other CDRs were

revealed to be novel sequences.

Sequence Listing

Seq. I.D. number : 1

Sequence length : 399

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..399

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..27

Characteristics determination method : S

Sequence

CTG TCG GTA ACT TCA GGG GTC TAC TCA GAG GTT CAG CTC CAG CAG TCT	48
Leu Ser Val Thr Ser Gly Val Tyr Ser Glu Val Gln Leu Gln Gln Ser	
-5 1 5	
GGG ACT GTG CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG TCC TGC AAG	96
Gly Thr Val Leu Ala Arg Pro Gly Ala Ser Val Lys Met Ser Cys Lys	
10 15 20	
GCT TCG GGC TAC ACC TTT AAC AGC TAC TGG ATG CAC TGG GTA AAA CAG	144
Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Trp Met His Trp Val Lys Gln	
25 30 35	
AGG CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG ATT TAT CCT GGA AAT	192
Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn	
40 45 50 55	
AGT GAT ATT AGC TAC AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG ACT	240
Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu Thr	
60 65 70	
GCC GTC ACA TCC ACC AGC ACT GCC TAC ATG GAA CTC AGA AGC CTG ACA	288
Ala Val Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu Thr	
75 80 85	
AAT GAG GAC TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA TAT GAT TAC	336
Asn Glu Asp Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu Tyr Asp Tyr	
90 95 100	
GAC ACC CTG GAC TAC TGG GGT CAA GGA ACC TCA GTC ACC GTC TCC TCA	384
Asp Thr Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser	
105 110 115	
GCC AAA ACG ACA CCC	399
Ala Lys Thr Thr Pro	
120	

Sequence Listing

Seq. I.D. number : 2

Sequence length : 402

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..402

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..30

Characteristics determination method : S

Sequence

ATT CTG TCG GTA ACT TCA GGG GTC TAC TCA GAG GTT CAG CTC CAG CAG 48

Ile Leu Ser Val Thr Ser Gly Val Tyr Ser Glu Val Gln Leu Gln Gln

-10 -5 1 5

TCT GGG ACT GTG CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG TCC TGC 96

Ser Gly Thr Val Leu Ala Arg Pro Gly Ala Ser Val Lys Met Ser Cys

10 15 20

AAG GCT TCG GGC TAC ACC TTT AAC AGC TAC TGG ATG CAC TGG GTA AAA 144

Lys Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Trp Met His Trp Val Lys

25 30 35

CAG AGG CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG ATT TAT CCT GGA 192

Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly

40 45 50

AAT AGT GAT ATT AGC TAC AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG 240

Asn Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu

55 60 65

ACT GCC GTC ACA TCC ACC AGC ACT GCC TAC ATG GAA CTC AGA AGC CTG 288

Thr Ala Val Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu

70 75 80 85

ACA AAT GAG GAC TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA TAT GAT 336

Thr Asn Glu Asp Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu Tyr Asn

90 95 100

TAC GAC ACC CTG GAC TAC TGG GGT CAA GGA ACC TCA GTC ACC GTC TGC 384

TVR ASP THR LEU ASP TVR TRP GLY GLN GLY THR SER VAL THR VAL SER

105 110 115

103 110 115

CA GCC AAA ALG ACA CCC
Ser Ala Lys Thr Thr Pro

133

120

Sequence Listing

Seq. I.D. number : 3

Sequence length : 438

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..438

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..57

Characteristics determination method : S

Sequence

```

25  ATG GAG TTC GGG CTA AAC TGG GTT TTC CTT GTA ACA CTT TTA AAT GGT 48
    Met Glu Phe Gly Leu Asn Trp Val Phe Leu Val Thr Leu Leu Asn Gly
        -15                -10                -5

    ATC CAG TGT GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC TTG GTA CAG 96
    Ile Gln Cys Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Gln
            1                5                10

30  CCT GGG GGT TCT CTC AGA CTC TCC TGT GCA ACT TCT GGG TTA ACC TTC 144
    Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Leu Thr Phe
        15                20                25

    ACT GAT TAC TAC ATG AAC TGG GTC CGC CAG CCT CCA GGA AAG GAA CTT 192
    Thr Asp Tyr Tyr Met Asn Trp Val Arg Gln Pro Pro Gly Lys Glu Leu
        30                35                40

35  GAA TGG TTG GGT TTT ATT AGA AAC AAA GCT AAT CTT TAC ACA ACA GAC 240
    Glu Trp Leu Gly Phe Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr Asp
        45                50                55                60

    TAC AGT GCA TCT GTG AAG GGT CGG TTC ACC ATC TCC AGA GAT AAT CCC 288
    Tyr Ser Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Pro
        65                70                75

    CAA AGC ATC CTC TAT CTT CAA ATG AAC ACC CTG ACA ACT GAG GAC AGT 336
    Gln Ser Ile Leu Tyr Leu Gln Met Asn Thr Leu Thr Thr Glu Asp Ser
        80                85                90

45  GCC ACT TAT TAC TGT GCA AGA GAT AGG GGG GGG AGG GAC TGG TAC TTC 384
    Ala Thr Tyr Tyr Cys Ala Arg Asp Arg Gly Gly Arg Asp Trp Tyr Phe
        95                100                105

    GAT GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA GCC AAA ACG 432
    Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys Thr
        110                115                120

50  ACA CCC 438
    Thr Pro
    125

```

Sequence Listing

Seq. I.D. number : 4

Sequence length : 411

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..411

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..30

Characteristics determination method : S

Sequence

25	CIT GTA ACA CGT TTA AAT GGT ATC CAG TGT GAG GTG AAG CTG GTG GAG	48
	Leu Val Thr Arg Leu Asn Gly Ile Gln Cys Glu Val Lys Leu Val Glu	
	-10 -5 1 5	
	TCT GGA GGA GGC TTG GTA CAG CCT GGG GGT TCT CTG AGA CTC TCC TGT	96
	Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys	
30	10 15 20	
	GCA ACT TCT GGG TTC ACC TTC ACT GAT TAC TAC ATG AAC TGG GTC CGC	144
	Ala Thr Ser Gly Phe Thr Phe Thr Asp Tyr Tyr Met Asn Trp Val Arg	
	25 30 35	
	CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG GGT TTT ATT AGA AAC AAA	192
35	Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu Gly Phe Ile Arg Asn Lys	
	40 45 50	
	GCT AAT TAT TAC ACA ACA GAG TAC AGT GCA TCT GTG AAG GGT CGG TTC	240
	Ala Asn Tyr Tyr Thr Thr Glu Tyr Ser Ala Ser Val Lys Gly Arg Phe	
	55 60 65	
40	ACC ATC TCC AGA GAT AAT TCC CAA AGC ATC CTC TAT CTT CAA ATG AAC	288
	Thr Ile Ser Arg Asp Asn Ser Gln Ser Ile Leu Tyr Leu Gln Met Asn	
	70 75 80 85	
	ACC CTG AGA GCT GAG GAC AGT GCC ACT TAT TAC TGT GCA AGA GAT GGG	336
45	Thr Leu Arg Ala Glu Asp Ser Ala Thr Tyr Tyr Cys Ala Arg Asp Gly	
	90 95 100	
	TTC CTA CGG GAC TGG TAC TTC GAT GTC TGG GGC GCA GGG ACC ACG GTC	384
	Phe Leu Arg Asp Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val	
	105 110 115	
50	ACC GTC TCC TCA GCC AAA ACG ACA CCC	411
	Thr Val Ser Ser Ala Lys Thr Thr Pro	
	120 125	

Sequence Listing

5 Seq. I.D. number : 5

Sequence length : 363

Sequence type : nucleic acid

10 Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

15 Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

20 Presence position : 1..363

Characteristics determination method : S

Sequence

25	GAG GTT CAG CTC CAG CAG TCT GGG GCT GAA CTG GCA AGA CCT GGG GCT	48
	Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala	
	1 5 10 15	
	TCA GTG AAC TTG TCC TGC AAG GCT TCT GGC TAC ACC TTT ACT AAC TAC	96
	Ser Val Asn Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr	
30	20 25 30	
	TGG ATG CAG TGG GTA AAA CAG AGG CGT GGA CAG GGT CTG GAA TGG ATT	144
	Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile	
	35 40 45	
35	GGG GCT ATT TAT CCT GGA GAT GGT GAT ACT AGG TAC ACT CAG AAG TTC	192
	Gly Ala Ile Tyr Pro Gly Asp Gly Asp Thr Arg Tyr Thr Gln Lys Phe	
	50 55 60	
	AAG GGC AAG GCC ACA TTG ACT GCA GCT AAA TCC TCC AGC ACA GCC TAC	240
40	Lys Gly Lys Ala Thr Leu Thr Ala Ala Lys Ser Ser Ser Thr Ala Tyr	
	65 70 75	
	ATG CAA CTC AGC AGC TTG GCA TCT GAG GAC TCT GCG GTC TAT TAC TGT	288
	Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys	
45	80 85 90 95	
	GCA AGA TCG GGC TAC TAT GGT AGC TTC GTT GGG TTT GCT TAC TGG GGC	336
	Ala Arg Ser Gly Tyr Tyr Gly Ser Phe Val Gly Phe Ala Tyr Trp Gly	
	100 105 110	
50	CAA GGG ACT CTG GTC ACT GTC TCT GCA	363
	Gln Gly Thr Leu Val Thr Val Ser Ala	
	115 120	

55

Sequence Listing

Seq. I.D. number : 6

Sequence length : 354

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..354

Characteristics determination method : S

Sequence

	GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CCT CTG	48
25	Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Pro Leu	
	1 5 10 15	
	GGG CAG AGG GCC ACC ATC TCA TAC AGG GCC AGC AAA AGT GTG CAG TTA	96
	Gly Gln Arg Ala Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Gln Leu	
30	20 25 30	
	CAT CTG GCT ATA GTT TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG	144
	His Leu Ala Ile Val Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln	
	35 40 45	
35	CCA CCC AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC	192
	Pro Pro Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val	
	50 55 60	
	CCT GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC	240
40	Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn	
	65 70 75	
	ATC CAT CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC	288
	Ile His Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His	
	80 85 90 95	
45	ATT AGG GTA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA	336
	Ile Arg Val Ala Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys	
	100 105 110	
	CGG GCT GAT GCT GCA CCA	354
50	Arg Ala Asp Ala Ala Pro	
	115	

Sequence Listing

Seq. I.D. number : 7

Sequence length : 438

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..438

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..39

Characteristics determination method : S

Sequence

```

25   CTA TGG GTA CTG CTG CTC TGG GTT CCA GGT TCC ACT GGT GAC ATT GTG   48
      Leu Trp Val Leu Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Ile Val
          -10          -5          1
      CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG CAG AGG GCC   96
      Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala
          5          10          15
30   TCC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT GGC TAT AGT   144
      Ser Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser
          20          25          30
      TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG CCA CCC AGA CTC CTC   192
      Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln Pro Pro Arg Leu Leu
          35          40          45          50
      ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC CCT GCC AGG TTC AGT   240
      Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val Pro Ala Arg Phe Ser
          55          60          65
40   GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT CCT GTG GAG   288
      Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu
          70          75          80
      GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT AGG GGA GCT TAC   336
      Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Arg Gly Ala Tyr
          85          90          95
45   ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA CGG GCT GAT GCT GCA   384
      Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Asp Ala Ala
          100          105          110
      CCA ACT GTA TCC ATC TTC CCA CCA TCC AGT AAG CTT GGG AAA CGG TTC   432
      Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Lys Leu Gly Lys Arg Phe
          115          120          125          130
50   GCA CCG
      Ala Pro

```

438

Sequence Listing

Seq. I.D. number : 8

Sequence length : 417

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 28..417

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 28..90

Characteristics determination method : S

Sequence

```

25      GGCCGCG GTGAGAACCG TTGGGAATTC ATG GAG ACA GAC ACA CTC CTG      48
                                         Met Glu Thr Asp Thr Leu Leu
                                         -20          -15

    CTA TGG GTA CTG CTG CTC TGG GTT CCA GGT TCC ACT GGT GAC ATT GTG      96
    Leu Trp Val Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Ile Val
    -10          -5          1

    CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG CAG AGG GCC      144
    Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala
    5          10          15

35    ACC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT GGC TAT AGT      192
    Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser
    20          25          30

    TAT ATG CAC TGG AAC CAA CAG AGA CCA GGA CAG CCA CCC AGA CTC CTC      240
    Tyr Met His Trp Asn Gln Gln Arg Pro Gly Gln Pro Pro Arg Leu Leu
    35          40          45          50

    ATC TAT CTT GTA TCC AAC CTA GAC TCT GGG GTC CCT GCC AGG TTC AGT      288
    Ile Tyr Leu Val Ser Asn Leu Asp Ser Gly Val Pro Ala Arg Phe Ser
    55          60          65

45    GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT CCT GTG GAG      336
    Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu
    70          75          80

    GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT GAG GGA GCT TAC      384
    Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Glu Gly Ala Tyr
    85          90          95

50    ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA      417
    Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
    100          105

```

Sequence Listing

Seq. I.D. number : 9

Sequence length : 420

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 31..420

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 31..90

Characteristics determination method : S

Sequence

```

25      GCGGCCGCGG TGAGAACCGT TTGGGAATTC ATG GAG ACA CAG TCC CAG      48
                                         Met Glu Thr Gln Ser Gln
                                         -20                      -15

GTC TTT GTA TTC GTG TTT CTC TGG TTG TCT GGT GTT GAC GGA GAC ATT      96
Val Phe Val Phe Val Phe Leu Trp Leu Ser Gly Val Asp Gly Asp Ile
30      -10                      -5                      1

GTG ATG ACC CAG TCT CAC AAA TTC ATG TCC ACA TCA GTA GGA GAC AGG      144
Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly Asp Arg
                        5                      10                      15

GTC AGT ATC ACC TGC AAG GCC AGT CAG GAT GTG AAT ACT GCT GTA GCC      192
Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala Val Ala
35      20                      25                      30

TGG TAT CAA CAG AAA CCA GGA CAA TCT CCT AAA CTA CTG CTT TAC TCG      240
Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Leu Tyr Ser
40      35                      40                      45

GCA TCC TAC CGG TAC ACT GGA GTC CCT GAT CAC TTC ACT GGC AGT GGA      288
Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp His Phe Thr Gly Ser Gly
50      50                      55                      60                      65

TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC GGT GTG CAG GCT GAA GAC      336
Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Gly Val Gln Ala Glu Asp
45      70                      75                      80

CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT AGT CCT CCT CTC ACG TTC      384
Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Pro Pro Leu Thr Phe
85                      90                      95

GGT GCT GGG ACC AAG CTG GAA CTG AAA CGG GCT GAT      420
Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Ala Asp
100                      105

```

Sequence Listing

Seq. I.D. number : 10

Sequence length : 360

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..360

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..12

Characteristics determination method : S

Sequence

	GGT GTT GAC GGA GAC ATT GTG ATG ACA CAG TCT CAC AAA TTC ATG TCC	48
	Gly Val Asp Gly Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser	
	1 5 10	
30	ACA TCA GTT GGA GAC AGG GTC ACC ATC ACC TGC AAG GCC AGT CAG GAT	96
	Thr Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp	
	15 20 25	
	GTG ACT ACT GAT GTA GCC TGG TAT CAA CAG AAA CCA CGA CAA TCT CCT	144
35	Val Thr Thr Asp Val Ala Trp Tyr Gln Gln Lys Pro Arg Gln Ser Pro	
	30 35 40	
	AAA CTA CTG ATT TAC TCG GCA TCC TAT CGG TAC ACT GGA GTC CCT GAT	192
	Lys Leu Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp	
	45 50 55	
40	CGC TTC ACT GGC AGT GGA TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC	240
	Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser	
	60 65 70 75	
	AGT GTG CAG GCT GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT	288
45	Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr	
	80 85 90	
	AGT ACT GCG TGG ACG TTC GGT GGT GGC ACC AAG CTG GAA ATC AAA CGG	336
	Ser Thr Ala Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg	
	95 100 105	
50	GCT GAT GCT GCA CCA ACT GTA TCC	360
	Ala Asp Ala Ala Pro Thr Val Ser	
	110 115	

SEQUENCE LISTING

5

(1) GENERAL INFORMATION:

(i) APPLICANT:

10

- (A) NAME:HAGIWARA, Yoshihide
- (B) STREET:4-14, Hiraisanso
- (C) CITY:Takarazuka-shi
- (D) STATE:Hyogo-ken
- (E) COUNTRY:Japan
- (F) POSTAL CODE (ZIP):none

15

(ii) TITLE OF INVENTION:AMINO ACID SEQUENCES OF ANTI-IDIOTYPIC ANTIBODIES AGAINST ANTI-CANCER HUMAN MONOCLONAL ANTIBODY, AND DNA BASE SEQUENCES ENCODING THOSE SEQUENCES

20

(iii) NUMBER OF SEQUENCES:48

(iv) COMPUTER READABLE FORM:

25

- (A) MEDIUM TYPE:Floppy disk
- (B) COMPUTER:IBM PC compatible
- (C) OPERATING SYSTEM:MS DOS 4.0
- (D) SOFTWARE:Microsoft Word, Version 5.5

(v) CURRENT APPLICATION DATA:

- (A) APPLICATION NUMBER:EP 94 115 683.8
- (B) FILING DATE:October 5, 1994

30

(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:

35

- (A) LENGTH:5 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

- (A) NAME/KEY:H-CDR1-1
- (D) OTHER INFORMATION:hypervariable region

40

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:1:

Ser Tyr Trp Met His

5

45

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:5 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

50

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

- (A) NAME/KEY:H-CDR1-2
- (D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 2:

55

Asp Tyr Tyr Met Asn

5

5

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:5 amino acids

(B) TYPE:amino acid

10

(D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

(A) NAME/KEY:H-CDR1-3

(D) OTHER INFORMATION:hypervariable region

15

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:3:

Asn Tyr Trp Met Gln

5

(2) INFORMATION FOR SEQ ID NO: 4:

20

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:17 amino acids

(B) TYPE:amino acid

(D) TOPOLOGY:linear

25

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

(A) NAME/KEY:H-CDR2-1

(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 4:

Ala Ile Tyr Pro Gly Asn Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys

30

5

10

15

Asp

(2) INFORMATION FOR SEQ ID NO: 5:

35

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:19 amino acids

(B) TYPE:amino acid

(D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

40

(A) NAME/KEY:H-CDR2-2

(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:5:

Phe Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr Asp Tyr Ser Ala Ser

45

5

10

15

Val Lys Gly

(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:

50

(A) LENGTH:19 amino acids

(B) TYPE:amino acid

(D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

55

- (A) NAME/KEY:H-CDR2-3
(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 6:

Phe Ile Arg Asn Lys Ala Asn Tyr Tyr Thr Thr Glu Tyr Ser Ala Ser
 5 10 15
Val Lys Gly

(2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:17 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

- (A) NAME/KEY:H-CDR2-4
(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:7:

Ala Ile Tyr Pro Gly Asp Gly Asp Thr Arg Tyr Thr Glu Lys Phe Lys
 5 10 15
Gly

(2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:10 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

- (A) NAME/KEY:H-CDR3-1
(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 8:

Glu Glu Tyr Asp Tyr Asp Thr Leu Asp Tyr
 5 10

(2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:11 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

- (A) NAME/KEY:H-CDR3-2
(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:9:

Asp Arg Gly Gly Arg Asp Trp Tyr Phe Asp Val
 5 10

(2) INFORMATION FOR SEQ ID NO: 10:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH:11 amino acids
 (B) TYPE:amino acid
 (D) TOPOLOGY:linear
 (ii) MOLECULE TYPE:protein
 (ix) FEATURE:
 (A) NAME/KEY:H-CDR3-3
 (D) OTHER INFORMATION:hypervariable region
 10 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 10:

Asp Gly Phe Leu Arg Asp Trp Tyr Phe Asp Val
 5 10

(2) INFORMATION FOR SEQ ID NO: 11:

- 15 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:12 amino acids
 (B) TYPE:amino acid
 (D) TOPOLOGY:linear
 20 (ii) MOLECULE TYPE:protein
 (ix) FEATURE:
 (A) NAME/KEY:H-CDR3-4
 (D) OTHER INFORMATION:hypervariable region
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO:11:

25 Ser Gly Tyr Tyr Gly Ser Phe Val Gly Phe Ala Tyr
 5 10

(2) INFORMATION FOR SEQ ID NO: 12:

- 30 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:17 amino acids
 (B) TYPE:amino acid
 (D) TOPOLOGY:linear
 (ii) MOLECULE TYPE:protein
 (ix) FEATURE:
 35 (A) NAME/KEY:L-CDR1-1
 (D) OTHER INFORMATION:hypervariable region
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 12:

40 Tyr Arg Ala Ser Lys Ser Val Gln Leu His Leu Ala Ile Val Tyr Met
 5 10 15
 His

(2) INFORMATION FOR SEQ ID NO: 13:

- 45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:16 amino acids
 (B) TYPE:amino acid
 (D) TOPOLOGY:linear
 (ii) MOLECULE TYPE:protein
 (ix) FEATURE:
 50 (A) NAME/KEY:L-CDR1-2
 (D) OTHER INFORMATION:hypervariable region
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO:13:

55 Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser Tyr Met His
 5 10 15

(2) INFORMATION FOR SEQ ID NO: 14:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:11 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

- (A) NAME/KEY:L-CDR1-3
- (D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 14:

Lys Ala Ser Gln Asp Val Asn Thr Ala Val Ala
5 10

(2) INFORMATION FOR SEQ ID NO: 15:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:11 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

- (A) NAME/KEY:L-CDR1-4
- (D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:15:

Lys Ala Ser Gln Asp Val Thr Thr Asp Val Ala
5 10

(2) INFORMATION FOR SEQ ID NO: 16:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:7 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

- (A) NAME/KEY:L-CDR2-1
- (D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 16:

Leu Val Ser Asn Leu Glu Ser
5

(2) INFORMATION FOR SEQ ID NO: 17:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:7 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

- (A) NAME/KEY:L-CDR2-2
- (D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:17:

L u Val Ser Asn Leu Asp Ser

5

(2) INFORMATION FOR SEQ ID NO: 18:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:7 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

(A) NAME/KEY:L-CDR2-3

(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 18:

Ser Ala Ser Tyr Arg Tyr Thr

5

(2) INFORMATION FOR SEQ ID NO: 19:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:8 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

(A) NAME/KEY:L-CDR3-1

(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:19:

Gln His Ile Arg Val Ala Tyr Thr

5

(2) INFORMATION FOR SEQ ID NO: 20:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:8 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

(A) NAME/KEY:L-CDR3-2

(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 20:

Gln His Ile Arg Gly Ala Tyr Thr

5

(2) INFORMATION FOR SEQ ID NO: 21:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:8 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

(A) NAME/KEY:L-CDR3-3

(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:21:

5 Gln His Ile Glu Gly Ala Tyr Thr
5

(2) INFORMATION FOR SEQ ID NO: 22:

10 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:9 amino acids
(B) TYPE:amino acid
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
15 (A) NAME/KEY:L-CDR3-4
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 22:

Gln Gln His Tyr Ser Pro Pro Leu Thr
5

20 (2) INFORMATION FOR SEQ ID NO: 23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:9 amino acids
(B) TYPE:amino acid
25 (D) TOPOLOGY:linear
(ii) MOLECULE TYPE:protein
(ix) FEATURE:
(A) NAME/KEY:L-CDR3-5
(D) OTHER INFORMATION:hypervariable region
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:23:

30 Gln Gln His Tyr Ser Thr Ala Trp Thr
5

(2) INFORMATION FOR SEQ ID NO: 24:

35 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:34 base pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:single
(D) TOPOLOGY:linear
40 (ii) MOLECULE TYPE:cDNA
(iv) ANTISENSE:no
(iii) HYPOTHETICAL:no
(ix) FEATURE:
(A) NAME/KEY:H Leader Sequence A
(D) OTHER INFORMATION:R is A or G;
45 S is C or G;
K is G or T;
Y is C or T;
M is A or C.
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 24:

50 GGGGAATTCAT GRASTTSKGG YYTMARCTKG RTTT

34

(2) INFORMATION FOR SEQ ID NO: 25:

(i) SEQUENCE CHARACTERISTICS:

55

5 (A) LENGTH:34 base pairs
 (B) TYPE:nucleic acid
 (C) STRANDEDNESS:single
 (D) TOPOLOGY:linear
 (ii) MOLECULE TYPE:cdna
 (iii) HYPOTHETICAL:no
 (iv) ANTISENSE:no
 (ix) FEATURE:
 10 (A) NAME/KEY:H Leader Sequence B
 (D) OTHER INFORMATION:S is C or G;
 Y is C or T;
 W is A or T;
 R is A or G.
 15 (xi) SEQUENCE DESCRIPTION:SEQ ID NO:25:

GGGAATTCAT GRAATGSASC TGGGTYWTYC TCTT

34

(2) INFORMATION FOR SEQ ID NO: 26:

20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:18 base pairs
 (B) TYPE:nucleic acid
 (C) STRANDEDNESS:single
 (D) TOPOLOGY:linear
 (ii) MOLECULE TYPE:cdna
 25 (iii) HYPOTHETICAL:no
 (iv) ANTISENSE:no
 (ix) FEATURE:
 (A) NAME/KEY:H Leader Sequence C
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 26:

30 TTAAATGGTA TCCAGTGT

18

(2) INFORMATION FOR SEQ ID NO: 27:

35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:35 base pairs
 (B) TYPE:nucleic acid
 (C) STRANDEDNESS:single
 (D) TOPOLOGY:linear
 (ii) MOLECULE TYPE:cdna
 (iii) HYPOTHETICAL:no
 40 (iv) ANTISENSE:no
 (ix) FEATURE:
 (A) NAME/KEY:H Constant Region
 (D) OTHER INFORMATION:R is A or G;
 K is G or T;
 N is inosine.
 45 (xi) SEQUENCE DESCRIPTION:SEQ ID NO:27:

CCCAAGCTTC CAGGGRCCAR KGGATARACN GRTGG

35

(2) INFORMATION FOR SEQ ID NO: 28:

50 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:32 base pairs
 (B) TYPE:nucleic acid
 (C) STRANDEDNESS:single
 (D) TOPOLOGY:linear

55

5 (ii) MOLECULE TYPE:cDNA
 (iii) HYPOTHETICAL:no
 (iv) ANTISENSE:no
 (ix) FEATURE:
 (A) NAME/KEY:L Leader Sequence A
 (D) OTHER INFORMATION:R is A or G;
 K is G or T;
 W is A or T;
 Y is C or T.
 10 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 28:

GGGAATTCAT GRAGWCACAK WCYCAGGTCT TT

32

15 (2) INFORMATION FOR SEQ ID NO: 29:
 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:33 base pairs
 (B) TYPE:nucleic acid
 (C) STRANDEDNESS:single
 (D) TOPOLOGY:linear
 20 (ii) MOLECULE TYPE:cDNA
 (iii) HYPOTHETICAL:no
 (iv) ANTISENSE:no
 (ix) FEATURE:
 (A) NAME/KEY:L Leader Sequence B
 25 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 29:

GGAATTCAAT GGAGACAGAC ACACTCCTGC TAT

33

(2) INFORMATION FOR SEQ ID NO: 30:
 30 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:30 base pairs
 (B) TYPE:nucleic acid
 (C) STRANDEDNESS:single
 (D) TOPOLOGY:linear
 35 (ii) MOLECULE TYPE:cDNA
 (iii) HYPOTHETICAL:no
 (iv) ANTISENSE:no
 (ix) FEATURE:
 (A) NAME/KEY:L constant
 40 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 30:

CCCAAGCTTA CTGGATGGTG GGAAGATGGA

30

(2) INFORMATION FOR SEQ ID NO: 31:
 45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:357 base pairs
 (B) TYPE:nucleic acid
 (C) STRANDEDNESS:double
 (D) TOPOLOGY:linear
 50 (ii) MOLECULE TYPE:mRNA
 (iii) HYPOTHETICAL:no
 (iv) ANTISENSE:no
 (vi) ORIGINAL SOURCE:
 (A) ORGANISM:mouse
 55 (ix) FEATURE:

(A) NAME/KEY:Idio 3 H chain variabl /Idio 17 H chain variable
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 31:

5 GAG GTT CAG CTC GAG CAG TCT GGG ACT GTG CTG GCA AGG CCT GGG GCT 48
 Glu Val Gln Leu Gln Gln Ser Gly Thr Val Leu Ala Arg Pro Gly Ala
 5 10 15

10 TCA GTG AAG ATG TCC TGC AAG GCT TCG GGC TAC ACC TTT AAC AGC TAC 96
 Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Asn Ser Tyr
 20 25 30

15 TGG ATG CAC TGG GTA AAA CAG AGG CCT GGA CAG GGT CTG GAA TGG ATT 144
 Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

20 GGC GCG ATT TAT CCT GGA AAT AGT GAT ATT AGC TAC AGC CAG AAC TTT 192
 Gly Ala Ile Tyr Pro Gly Asn Ser Asp Ile Ser Tyr Ser Gln Asn Phe
 50 55 60

25 AAG GAC AGG GCC AAA CTG ACT GCC GTC ACA TCC ACC AGC ACT GCC TAC 240
 Lys Asp Arg Ala Lys Leu Thr Ala Val Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

30 ATG GAA CTC AGA AGC CTG ACA AAT GAG GAC TCT GCG GTC TAT TTC TGT 288
 Met Glu Leu Arg Ser Leu Thr Asn Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95

35 ACA AAA GAG GAA TAT GAT TAC GAC ACC CTG GAC TAC TGG GGT CAA GGA 336
 Thr Lys Glu Glu Tyr Asp Tyr Asp Thr Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

40 ACC TCA GTC ACC GTC TCC TCA 357
 Thr Ser Val Thr Val Ser Ser
 115

(2) INFORMATION FOR SEQ ID NO: 32:

35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:366 base pairs
 (B) TYPE:nucleic acid
 (C) STRANDEDNESS:double
 (D) TOPOLOGY:linear

40 (ii) MOLECULE TYPE:mRNA
 (iii) HYPOTHETICAL:no
 (iv) ANTISENSE:no
 (vi) ORIGINAL SOURCE:
 (A) ORGANISM:mouse

45 (ix) FEATURE:
 (A) NAME/KEY:Idio 20 H chain variable
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 32:

50 GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC TTG GTA CAG CCT GGG GGT 48
 Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 5 10 15

55 TCT CTC AGA CTC TCC TGT GCA ACT TCT GGG TTA ACC TTC ACT GAT TAC 96
 Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Leu Thr Phe Thr Asp Tyr
 20 25 30

55

5 TAC ATG AAC TGG GTC CGC CAG CCT CCA GGA AAG GAA CTT GAA TGG TTG 144
Tyr Met Asn Trp Val Arg Gln Pro Pro Gly Lys Glu Leu Glu Trp Leu
35 40 45

GGT TTT ATT AGA AAC AAA GCT AAT CTT TAC ACA ACA GAC TAC AGT GCA 192
Gly Phe Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr Asp Tyr Ser Ala
50 55 60

10 TCT GTG AAG GGT CGG TTC ACC ATC TCC AGA CAT AAT CCC CAA AGC ATC 240
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Pro Gln Ser Ile
65 70 75 80

CTC TAT CTT CAA ATG AAC ACC CTG ACA ACT GAG GAC AGT GCC ACT TAT 288
Leu Tyr Leu Gln Met Asn Thr Leu Thr Thr Glu Asp Ser Ala Thr Tyr
85 90 95

15 TAC TGT GCA AGA GAT AGG GGG GGG AGG GAC TGG TAC TTC GAT GTC TGG 336
Tyr Cys Ala Arg Asp Arg Gly Gly Arg Asp Trp Tyr Phe Asp Val Trp
100 105 110

20 GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA 366
Gly Ala Gly Thr Thr Val Thr Val Ser Ser
115 120

(2) INFORMATION FOR SEQ ID NO: 33:
(i) SEQUENCE CHARACTERISTICS:
25 (A) LENGTH:366 base pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:double
(D) TOPOLOGY:linear
(ii) MOLECULE TYPE:mRNA
(iii) HYPOTHETICAL:no
30 (iv) ANTISENSE:no
(vi) ORIGINAL SOURCE:
(A) ORGANISM:mouse
(ix) FEATURE:
(A) NAME/KEY:Idio 27 H chain variable
35 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 33:

GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC TTG GTA CAG CCT GGG GGT 48
Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
5 10 15

40 TCT CTG AGA CTC TCC TGT GCA ACT TCT GGG TTC ACC TTC ACT GAT TAC 96
Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Phe Thr Phe Thr Asp Tyr
20 25 30

TAC ATG AAC TGG GTC CGC CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG 144
Tyr Met Asn Trp Val Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu
35 40 45

GGT TTT ATT AGA AAC AAA GCT AAT TAT TAC ACA ACA GAG TAC AGT GCA 192
Gly Phe Ile Arg Asn Lys Ala Asn Tyr Tyr Thr Thr Glu Tyr Ser Ala
50 55 60

50

55

5 TCT GTG AAG GGT CGG TTC ACC ATC TCC AGA GAT AAT TCC CAA AGC ATC 240
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Gln Ser Ile 80
 65 70 75

CTC TAT CTT CAA ATG AAC ACC CTG AGA GCT GAG GAC AGT GCC ACT TAT 288
 Leu Gln Met Asn Thr Leu Thr Leu Arg Ala Glu Asp Ser Ala Thr Tyr 95
 85 90

10 TAC TGT GCA AGA GAT GGG TTC CTA CGG GAC TGG TAC TTC GAT GTC TGG 336
 Tyr Cys Ala Arg Asp Gly Phe Leu Arg Asp Trp Tyr Phe Asp Val Trp 110
 100 105

GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA 366
 Gly Ala Gly Thr Thr Val Thr Val Ser Ser 115 120
 15

(2) INFORMATION FOR SEQ ID NO: 34:

20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:363 base pairs
 (B) TYPE:nucleic acid
 (C) STRANDEDNESS:double
 (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA
 (iii) HYPOTHETICAL:no
 25 (iv) ANTISENSE:no
 (vi) ORIGINAL SOURCE:
 (A) ORGANISM:mouse
 (ix) FEATURE:
 (A) NAME/KEY:Idio 33 H chain variable
 30 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 34:

GAG GTT CAG CTC CAG CAG TCT GGG GCT GAA CTG GCA AGA CCT GGG GCT 48
 Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala 15
 5 10

35 TCA GTG AAC TTG TCC TGC AAG GCT TCT GGC TAC ACC TTT ACT AAC TAC 96
 Ser Val Asn Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr 30
 20 25

TGG ATG CAG TGG GTA AAA CAG AGG CCT GGA CAG GGT CTG GAA TGG ATT 144
 Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile 45
 35 40 45

GGG GCT ATT TAT CCT GGA GAT GGT GAT ACT AGG TAC ACT CAG AAG TTC 192
 Gly Ala Ile Tyr Pro Gly Asp Gly Asp Thr Arg Tyr Thr Gln Lys Phe 50 55 60

45 AAG GGC AAG GCC ACA TTG ACT GCA GCT AAA TCC TCC AGC ACA GCC TAC 240
 Lys Gly Lys Ala Thr Leu Thr Ala Ala Lys Ser Ser Ser Thr Ala Tyr 80
 65 70 75

ATG CAA CTC AGC AGC TTG GCA TCT GAG GAC TCT GCG GTC TAT TAC TGT 288
 Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys 85 90 95
 50

55

5 GCA AGA TCG GGC TAC TAT GGT AGC TTC GTT GGG TTT GCT TAC TGG GGC 336
Ala Arg Ser Gly Tyr Tyr Gly Ser Phe Val Gly Phe Ala Tyr Trp Gly
100 105 110

CAA GGG ACT CTG GTC ACT GTC TCT GCA 363
Gln Gly Thr Leu Val Thr Val Ser Ala
115 120

10

(2) INFORMATION FOR SEQ ID NO: 35:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:336 base pairs
 (B) TYPE:nucleic acid
 (C) STRANDEDNESS:double
 (D) TOPOLOGY:linear
 (ii) MOLECULE TYPE:mRNA
 (iii) HYPOTHETICAL:no
 (iv) ANTISENSE:no
 (vi) ORIGINAL SOURCE:
 (A) ORGANISM:mouse
 (ix) FEATURE:
 (A) NAME/KEY:Idio 3 L chain variable
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 35:

25 GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CCT CTG 48
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Pro Leu
5 10 15

30 GGG CAG AGG GCC ACC ATC TCA TAC AGG GCC AGC AAA AGT GTG CAG TTA 96
Gly Gln Arg Ala Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Gln Leu
20 25 30

CAT CTG GCT ATA GTT TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG 144
His Leu Ala Ile Val Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln
35 40 45

35 CCA CCC AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC 192
Pro Pro Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val
50 55 60

40 CCT GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC 240
Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn
65 70 75 80

45 ATC CAT CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC 288
Ile His Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His
85 90 95

ATT AGG GTA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA 336
Ile Arg Val Ala Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

50

(2) INFORMATION FOR SEQ ID NO: 36:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:330 base pairs

55

(B) TYPE:nucleic acid
 (C) STRANDEDNESS:double
 (D) TOPOLOGY:linear
 (ii) MOLECULE TYPE:mRNA
 (iii) HYPOTHETICAL:no
 (iv) ANTISENSE:no
 (vi) ORIGINAL SOURCE:
 (A) ORGANISM:mouse
 (ix) FEATURE:
 (A) NAME/KEY:Idio 17 L chain variable
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 36:

GAC	ATT	GTG	CTG	ACA	CAG	TCT	CCT	GCT	TCC	TTA	GCT	GTA	TCT	CTG	GGG	48
Asp	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Ser	Leu	Ala	Val	Ser	Leu	Gly	
				5					10					15		
CAG	AGG	GCC	TCC	ATC	TCA	TAC	AGG	GCC	AGC	AAA	AGT	GTC	AGT	ACA	TCT	96
Gln	Arg	Ala	Ser	Ile	Ser	Tyr	Arg	Ala	Ser	Lys	Ser	Val	Ser	Thr	Ser	
			20					25					30			
GGC	TAT	AGT	TAT	ATG	CAC	TGG	AAC	CAA	CAG	AAA	CCA	GGA	CAG	CCA	CCC	144
Gly	Tyr	Ser	Tyr	Met	His	Trp	Asn	Gln	Gln	Lys	Pro	Gly	Gln	Pro	Pro	
		35					40					45				
AGA	CTC	CTC	ATC	TAT	CTT	GTA	TCC	AAC	CTA	GAA	TCT	GGG	GTC	CCT	GCC	192
Arg	Leu	Leu	Ile	Tyr	Leu	Val	Ser	Asn	Leu	Glu	Ser	Gly	Val	Pro	Ala	
	50					55					60					
AGG	TTC	AGT	GGC	AGT	GGG	TCT	GGG	ACA	GAC	TTC	ACC	CTC	AAC	ATC	CAT	240
Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Asn	Ile	His	
65				70					75					80		
CCT	GTG	GAG	GAG	GAG	GAT	GCT	GCA	ACC	TAT	TAC	TGT	CAG	CAC	ATT	AGG	288
Pro	Val	Glu	Glu	Glu	Asp	Ala	Ala	Thr	Tyr	Tyr	Cys	Gln	His	Ile	Arg	
			85					90					95			
GGA	GCT	TAC	ACG	TTC	GGA	GGG	GGG	ACC	AAG	CTG	GAA	ATA	AAA			330
Gly	Ala	Tyr	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys			
			100					105					110			

(2) INFORMATION FOR SEQ ID NO: 37:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:330 base pairs
 (B) TYPE:nucleic acid
 (C) STRANDEDNESS:double
 (D) TOPOLOGY:linear
 (ii) MOLECULE TYPE:mRNA
 (iii) HYPOTHETICAL:no
 (iv) ANTISENSE:no
 (vi) ORIGINAL SOURCE:
 (A) ORGANISM:mouse
 (ix) FEATURE:
 (A) NAME/KEY:Idio 20 L chain variable
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 37:

5 GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG 48
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly 15

10 CAG AGG GCC ACC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT 96
Gln Arg Ala Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser 20 25 30

15 GGC TAT AGT TAT ATG CAC TGG AAC CAA CAG AGA CCA GGA CAG CCA CCC 144
Gly Tyr Ser Tyr Met His Trp Asn Gln Gln Arg Pro Gly Gln Pro Pro 35 40 45

20 AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAC TCT GGG GTC CCT GCC 192
Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Asp Ser Gly Val Pro Ala 50 55 60

25 AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT 240
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His 65 70 75 80

30 CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT GAG 288
Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Glu 85 90 95

35 GGA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA 330
Gly Ala Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys 100 105 110

(2) INFORMATION FOR SEQ ID NO: 38:

- 30 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:321 base pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:double
(D) TOPOLOGY:linear
- 35 (ii) MOLECULE TYPE:mRNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(vi) ORIGINAL SOURCE:
(A) ORGANISM:mouse
- 40 (ix) FEATURE:
(A) NAME/KEY:Idio 27 L chain variable
- (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 38:

45 GAC ATT GTG ATG ACC CAG TCT CAC AAA TTC ATG TCC ACA TCA GTA GGA 48
Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly 5 10 15

50 GAC AGG GTC AGT ATC ACC TGC AAG GCC AGT CAG GAT GTG AAT ACT GCT 96
Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala 20 25 30

55 GTA GCC TGG TAT CAA CAG AAA CCA GGA CAA TCT CCT AAA CTA CTG CTT 144
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Leu 35 40 45

5 TAC TCG GCA TCC TAC CGG TAC ACT GGA GTC CCT GAT CAC TTC ACT GGC 192
 Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp His Phe Thr Gly
 50 55 60

AGT GGA TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC GGT GTG CAG GCT 240
 Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Gly Val Gln Ala
 65 70 75 80

10 GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT AGT CCT CCT CTC 288
 Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Pro Pro Leu
 85 90 95

15 ACG TTC GGT GCT GGG ACC AAG CTG GAA CTG AAA 321
 Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
 100 105

(2) INFORMATION FOR SEQ ID NO: 39:

20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:321 base pairs
 (B) TYPE:nucleic acid
 (C) STRANDEDNESS:double
 (D) TOPOLOGY:linear

25 (ii) MOLECULE TYPE:mRNA
 (iii) HYPOTHETICAL:no
 (iv) ANTISENSE:no
 (vi) ORIGINAL SOURCE:
 (A) ORGANISM:mouse
 (ix) FEATURE:
 (A) NAME/KEY:Idio 33 L chain variable

30 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 39:

GAC ATT GTG ATG ACA CAG TCT CAC AAA TTC ATG TCC ACA TCA GTT GGA 48
 Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
 5 10 15

35 GAC AGG GTC ACC ATC ACC TGC AAG GCC AGT CAG GAT GTG ACT ACT GAT 96
 Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Thr Thr Asp
 20 25 30

40 GTA GCC TGG TAT CAA CAG AAA CCA CGA CAA TCT CCT AAA CTA CTG ATT 144
 Val Ala Trp Tyr Gln Gln Lys Pro Arg Gln Ser Pro Lys Leu Leu Ile
 35 40 45

TAC TCG GCA TCC TAT CGG TAC ACT GGA GTC CCT GAT CGC TTC ACT GGC 192
 Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
 50 55 60

45 AGT GGA TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC AGT GTG CAG GCT 240
 Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Val Gln Ala
 65 70 75 80

50 GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT AGT ACT GCG TGG 288
 Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Thr Ala Trp
 85 90 95

55

ACG TTC GGT GGT GGC ACC AAG CTG GAA ATC AAA
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Il Lys
 100 105

321

(2) INFORMATION FOR SEQ ID NO: 40:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:399 base pairs
 (B) TYPE:nucleic acid
 (C) STRANDEDNESS:double
 (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:

- (A) ORGANISM:mouse

(ix) FEATURE:

- (A) NAME/KEY:Clone 3GB1

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:40:

CTG TCG GTA ACT TCA GGG GTC TAC TCA GAG GTT CAG CTC GAG CAG TCT -48
 Leu Ser Val Thr Ser Gly Val Tyr Ser Glu Val Gln Leu Gln Gln Ser
 -5 1 5

GGG ACT GTG CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG TCC TGC AAG 96
 Gly Thr Val Leu Ala Arg Pro Gly Ala Ser Val Lys Met Ser Cys Lys
 10 15 20

GCT TCG GGC TAC ACC TTT AAC AGC TAC TGG ATG CAC TGG GTA AAA CAG 144
 Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Trp Met His Trp Val Lys Gln
 25 30 35

AGG CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG ATT TAT CCT GGA AAT 192
 Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn
 40 45 50 55

AGT GAT ATT AGC TAC AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG ACT 240
 Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu Thr
 60 65 70

GCC GTC ACA TCC ACC AGC ACT GCC TAC ATG GAA CTC AGA AGC CTG ACA 288
 Ala Val Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu Thr
 75 80 85

AAT GAG GAC TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA TAT GAT TAC 336
 Asn Glu Asp Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu Tyr Asp Tyr
 90 95 100

GAC ACC CTG GAC TAC TGG GGT CAA GGA ACC TCA GTC ACC GTC TCC TCA 384
 Asp Thr Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
 105 110 115

GCC AAA ACG ACA CCC 399
 Ala Lys Thr Thr Pro
 120

(2) INFORMATION FOR SEQ ID NO: 41:

- 5 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:402 base pairs
 (B) TYPE:nucleic acid
 (C) STRANDEDNESS:double
 (D) TOPOLOGY:linear
 10 (ii) MOLECULE TYPE:mRNA
 (iii) HYPOTHETICAL:no
 (iv) ANTISENSE:no
 (vi) ORIGINAL SOURCE:
 (A) ORGANISM:mouse
 (ix) FEATURE:
 (A) NAME/KEY:Clone 17GB7
 15 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 41:

```

ATT GTG TCG GTA ACT TCA GGG GTC TAC TCA GAG GTT CAG CTC GAG CAG 48
Ile Leu Ser Val Thr Ser Gly Val Tyr Ser Glu Val Gln Leu Gln Gln
-10 -5 1 5

20 TCT GGG ACT GTG CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG TCC TGC 96
Ser Gly Thr Val Leu Ala Arg Pro Gly Ala Ser Val Lys Met Ser Cys
10 15 20

25 AAG GCT TCG GGC TAC ACC TTT AAC AGC TAC TGG ATG CAC TGG GTA AAA 144
Lys Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Trp Met His Trp Val Lys
25 30 35

30 CAG AGG CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG ATT TAT CCT GGA 192
Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly
40 45 50

AAT AGT GAT ATT AGC TAC AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG 240
Asn Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu
55 60 65 70

35 ACT GCC GTC ACA TCC ACC AGC ACT GCC TAC ATG GAA CTC AGA AGC CTG 288
Thr Ala Val Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu
75 80 85

ACA AAT GAG GAC TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA TAT GAT 336
Thr Asn Glu Asp Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu Tyr Asp
90 95 100

40 TAC GAC ACC CTG GAC TAC TGG GGT CAA GGA ACC TCA GTC ACC GTC TCC 384
Tyr Asp Thr Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
105 110 115

45 TCA GCC AAA ACG ACA CCC 402
Ser Ala Lys Thr Thr Pro
120

```

(2) INFORMATION FOR SEQ ID NO: 42:

- 50 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:438 base pairs
 (B) TYPE:nucleic acid
 55

(C) STRANDEDNESS:double
 (D) TOPOLOGY:linear

5 (ii) MOLECULE TYPE:mRNA
 (iii) HYPOTHETICAL:no
 (iv) ANTISENSE:no
 (vi) ORIGINAL SOURCE:
 (A) ORGANISM:mouse

10 (ix) FEATURE:
 (A) NAME/KEY:Clone 20GA2
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO:42:

ATG GAG TTC GGG CTA AAC TGG GTT TTC CTT GTA ACA CTT TTA AAT GGT 48
 Met Glu Phe Gly Leu Asn Trp Val Phe Leu Val Thr Leu Leu Asn Gly
 -15 -10 -5

15 ATC CAG TGT GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC TTG GTA CAG 96
 Ile Gln Cys Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Gln
 1 5 10

20 CCT GGG GGT TCT CTC AGA CTC TCC TGT GCA ACT TCT GGG TTA ACC TTC 144
 Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Leu Thr Phe
 15 20 25

25 ACT GAT TAC TAC ATG AAC TGG GTC CGC CAG CCT CCA GGA AAG GAA CTT 192
 Thr Asp Tyr Tyr Met Asn Trp Val Arg Gln Pro Pro Gly Lys Glu Leu
 30 35 40 45

GAA TGG TTG GGT TTT ATT AGA AAC AAA GCT AAT CTT TAC ACA ACA GAC 240
 Glu Trp Leu Gly Phe Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr Asp
 50 55 60

30 TAC AGT GCA TCT GTG AAG GGT CGG TTC ACC ATC TCC AGA CAT AAT CCC 288
 Tyr Ser Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Pro
 65 70 75

35 CAA AGC ATC CTC TAT CTT CAA ATG AAC ACC CTG ACA ACT GAG GAC AGT 336
 Gln Ser Ile Leu Tyr Leu Gln Met Asn Thr Leu Thr Thr Glu Asp Ser
 80 85 90

GCC ACT TAT TAC TGT GCA AGA GAT AGG GGG GGG AGG GAC TGG TAC TTC 384
 Ala Thr Tyr Tyr Cys Ala Arg Asp Arg Gly Gly Arg Asp Trp Tyr Phe
 95 100 105

40 GAT GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA GCC AAA ACG 432
 Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys Thr
 110 115 120 125

45 ACA CCC 438
 Thr Pro

(2) INFORMATION FOR SEQ ID NO: 43:

50 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:411 base pairs
 (B) TYPE:nucleic acid
 (C) STRANDEDNESS:double
 (D) TOPOLOGY:linear

55

(ii) MOLECULE TYPE:mRNA
 (iii) HYPOTHETICAL:no
 5 (iv) ANTISENSE:no
 (vi) ORIGINAL SOURCE:
 (A) ORGANISM:mouse
 (ix) FEATURE:
 (A) NAME/KEY:Clone 27GA5
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 43:

10 CTT GTA ACA CGT TTA AAT GGT ATC CAG TGT GAG GTG AAG CTG GTG GAG 48
 Leu Val Thr Arg Leu Asn Gly Ile Gln Cys Glu Val Lys Leu Val Glu
 -10 -5 1 5

15 TCT GGA GGA GGC TTG GTA CAG CCT GGG GGT TCT CTG AGA CTC TCC TGT 96
 Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys
 10 15 20

20 GCA ACT TCT GGG TTC ACC TTC ACT GAT TAC TAC ATG AAC TGG GTC CGC 144
 Ala Thr Ser Gly Phe Thr Phe Thr Asp Tyr Tyr Met Asn Trp Val Arg
 25 30 35

25 CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG GGT TTT ATT AGA AAC AAA 192
 Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu Gly Phe Ile Arg Asn Lys
 40 45 50

30 GCT AAT TAT TAC ACA ACA GAG TAC AGT GCA TCT GTG AAG GGT CGG TTC 240
 Ala Asn Tyr Tyr Thr Thr Glu Tyr Ser Ala Ser Val Lys Gly Arg Phe
 55 60 65 70

35 ACC ATC TCC AGA GAT AAT TCC CAA AGC ATC CTC TAT CTT CAA ATG AAC 288
 Thr Ile Ser Arg Asp Asn Ser Gln Ser Ile Leu Gln Met Asn Thr Leu
 75 80 85

40 ACC CTG AGA GCT GAG GAC AGT GCC ACT TAT TAC TGT GCA AGA GAT GGG 336
 Thr Leu Arg Ala Glu Asp Ser Ala Thr Tyr Tyr Cys Ala Arg Asp Gly
 90 95 100

45 TTC CTA CGG GAC TGG TAC TTC GAT GTC TGG GGC GCA GGG ACC ACG GTC 384
 Phe Leu Arg Asp Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val
 105 110 115

50 ACC GTC TCC TCA GCC AAA ACG ACA CCC 411
 Thr Val Ser Ser Ala Lys Thr Thr Pro
 120 125

(2) INFORMATION FOR SEQ ID NO: 44:

45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:354 base pairs
 (B) TYPE:nucleic acid
 (C) STRANDEDNESS:double
 (D) TOPOLOGY:linear

50 (ii) MOLECULE TYPE:mRNA
 (iii) HYPOTHETICAL:no
 (iv) ANTISENSE:no
 (vi) ORIGINAL SOURCE:
 (A) ORGANISM:mouse

55

(ix) FEATURE:
(A) NAME/KEY:Clone 3KB11

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:44:

GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CCT CTG	48
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Pro Leu	
5 10 15	
GGG CAG AGG GCC ACC ATC TCA TAC AGG GCC AGC AAA AGT GTG CAG TTA	96
Gly Gln Arg Ala Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Gln Leu	
20 25 30	
CAT CTG GCT ATA GTT TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG	144
His Leu Ala Ile Val Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln	
35 40 45	
CCA CCC AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC	192
Pro Pro Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val	
50 55 60	
CCT GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC	240
Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn	
65 70 75 80	
ATC CAT CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC	288
Ile His Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His	
85 90 95	
ATT AGG GTA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA	336
Ile Arg Val Ala Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys	
100 105 110	
CGG GCT GAT GCT GCA CCA	354
Arg Ala Asp Ala Ala Pro	
115	

(2) INFORMATION FOR SEQ ID NO: 45:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:438 base pairs
(B) TYPE:nucleic acid
(C) STANDEDNESS:double
(D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:

(A) ORGANISM:mouse

(ix) FEATURE:

(A) NAME/KEY:Clone 17KB1

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 45:

CTA TGG GTA CTG CTG CTC TGG GTT CCA GGT TCC ACT GGT GAC ATT GTG	48
Leu Trp Val Leu Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Ile Val	
-10 -5 1	

5 CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG CAG AGG GCC 96
 Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala
 5 10 15
 10 TCC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT GGC TAT AGT 144
 Ser Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser
 20 25 30 35
 10 TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG CCA CCC AGA CTC CTC 192
 Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln Pro Pro Arg Leu Leu
 40 45 50
 15 ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC CCT GCC AGG TTC AGT 240
 Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val Pro Ala Arg Phe Ser
 55 60 65
 GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT CCT GTG GAG 288
 Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu
 70 75 80
 20 GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT AGG GGA GCT TAC 336
 Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Arg Gly Ala Tyr
 85 90 95
 25 ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA CGG GCT GAT GCT GCA 384
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Asp Ala Ala
 100 105 110 115
 CCA ACT GTA TCC ATC TTC CCA CCA TCC AGT AAG CTT GGG AAA CGG TTC 432
 Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Lys Leu Gly Lys Arg Phe
 120 125 130
 30 GCA CCG 438
 Ala Pro

(2) INFORMATION FOR SEQ ID NO: 46:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:417 base pairs
- (B) TYPE:nucleic acid
- (C) STRANDEDNESS:double
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:

- (A) ORGANISM:mouse

(ix) FEATURE:

- (A) NAME/KEY:Clone 20KB1

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:46:

GGCCGCG GTGAGAACCG TTGGGAATTC ATG GAG ACA GAC ACA CTC CTG 48
 Met Glu Thr Asp Thr Leu Leu
 -20 -15

5 CTA TGG GTA CTG CTG CTC TGG GTT CCA GGT TCC ACT GGT GAC ATT GTG 96
 Leu Trp Val Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Ile Val
 -10 -5 1
 CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG CAG AGG GCC 144
 Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala
 5 10 15
 10 ACC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT GGC TAT AGT 192
 Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser
 20 25 30
 15 TAT ATG CAC TGG AAC CAA CAG AGA CCA GGA CAG CCA CCC AGA CTC CTC 240
 Tyr Met His Trp Asn Gln Arg Pro Gly Gln Pro Pro Arg Leu Leu
 35 40 45
 ATC TAT CTT GTA TCC AAC CTA GAC TCT GGG GTC CCT GCC AGG TTC AGT 288
 Ile Tyr Leu Val Ser Asn Leu Asp Ser Gly Val Pro Ala Arg Phe Ser
 50 55 60 65
 20 GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT CCT GTG GAG 336
 Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu
 70 75 80
 25 GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT GAG GGA GCT TAC 384
 Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Glu Gly Ala Tyr
 85 90 95
 ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA 417
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105
 30

(2) INFORMATION FOR SEQ ID NO: 47:

- 35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH:420 base pairs
 (B) TYPE:nucleic acid
 (C) STRANDEDNESS:single
 (D) TOPOLOGY:linear
 (ii) MOLECULE TYPE:mRNA
 (iii) HYPOTHETICAL:no
 40 (iv) ANTISENSE:no
 (vi) ORIGINAL SOURCE:
 (A) ORGANISM:mouse
 (ix) FEATURE:
 (A) NAME/KEY:Clone 27KA2
 45 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 47:

GCGGCCGCGG TGAGAACCGT TTGGGAATTC ATC GAG ACA CAG TCC CAG 48
 Met Glu Thr Gln Ser Gln
 -20 -15
 50 GTC TTT GTA TTC GTG TTT CTC TGG TTG TCT GGT GTT GAC GGA GAC ATT 96
 Val Phe Val Phe Val Phe Leu Trp Leu Ser Gly Val Asp Gly Asp Ile
 -10 -5 1

55

5 GTG ATG ACC CAG TCT CAC AAA TTC ATG TCC ACA TCA GTA GGA GAC AGG 144
Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly Asp Arg
5 10 15

GTC AGT ATC ACC TGC AAG GCC AGT CAG GAT GTG AAT ACT GCT GTA GCC 192
Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala Val Ala
20 25 30

10 TGG TAT CAA CAG AAA CCA GGA CAA TCT CCT AAA CTA CTG CTT TAC TCG 240
Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Leu Tyr Ser
35 40 45 50

15 GCA TCC TAC CGG TAC ACT GGA GTC CCT GAT CAC TTC ACT GGC AGT GGA 288
Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp His Phe Thr Gly Ser Gly
55 60 65

TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC GGT GTG CAG GCT GAA GAC 336
Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Gly Val Gln Ala Glu Asp
70 75 80

20 CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT AGT CCT CCT CTC ACG TTC 384
Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Pro Pro Leu Thr Phe
85 90 95

25 GGT GCT GGG ACC AAG CTG GAA CTG AAA CGG GCT GAT 420
Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Ala Asp
100 105 110

(2) INFORMATION FOR SEQ ID NO: 48:

30 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH:360 base pairs
(B) TYPE:nucleic acid
(C) STRANDEDNESS:single
(D) TOPOLOGY:linear

35 (ii) MOLECULE TYPE:mRNA
(iii) HYPOTHETICAL:no
(iv) ANTISENSE:no
(vi) ORIGINAL SOURCE:
(A) ORGANISM:mouse
(ix) FEATURE:
(A) NAME/KEY:Clone 23KA26
40 (xi) SEQUENCE DESCRIPTION:SEQ ID NO:48

45 GGT GTT GAC GGA GAC ATT GTG ATG ACA CAG TCT CAC AAA TTC ATG TCC 48
Gly Val Asp Gly Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser
1 5 10

ACA TCA GTT GGA GAC AGG GTC ACC ATC ACC TGC AAG GCC AGT CAG GAT 96
Thr Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp
15 20 25

50 GTG ACT ACT GAT GTA GCC TGG TAT CAA CAG AAA CCA CGA CAA TCT CCT 144
Val Thr Thr Asp Val Ala Trp Tyr Gln Gln Lys Pro Arg Gln Ser Pro
30 35 40

55

AAA CTA CTG ATT TAC TCG GCA TCC TAT CGG TAC ACT GGA GTC CCT GAT 192
 Lys Leu Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp
 5 45 50 55
 CGC TTC ACT GGC AGT GGA TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC 240
 Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser
 60 65 70 75
 10 AGT GTG CAG GCT GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT 288
 Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr
 80 85 90
 15 AGT ACT GCG TGG ACG TTC GGT GGT GGC ACC AAG CTG GAA ATC AAA CCG 336
 Ser Thr Ala Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
 95 100 105
 GCT GAT GCT GCA CCA ACT GTA TCC 360
 Ala Asp Ala Ala Pro Thr Val Ser
 110 115

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25 Claims

1. An immunoglobulin H chain variable region fragment which contains a hypervariable region CDR1 having an amino acid sequence selected from

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(1) Ser Tyr Trp Met His;
 Asp Tyr Tyr Met Asn; and
 Asn Tyr Trp Met Gln,

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a hypervariable region CDR2 having an amino acid sequence selected from

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(2) Ala Ile Tyr Pro Gly Asn Ser
 Asp Ile Ser Tyr Ser Gln Asn
 Phe Lys Asp;

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Phe Ile Arg Asn Lys Ala
 Asn Leu Tyr Thr Thr Asp
 Tyr Ser Ala Ser Val Lys
 Gly;

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Phe Ile Arg Asn Lys Ala
 Asn Tyr Tyr Thr Thr Glu
 Tyr Ser Ala Ser Val Lys
 Gly; and

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Ala Ile Tyr Pro Gly Asp
 Gly Asp Thr Arg Tyr Thr
 Gln Lys Phe Lys Gly,

and a hypervariable region CDR3 having an amino acid sequence selected from

(3) Glu Glu Tyr Asp Tyr Asp
 Thr Leu Asp Tyr;
 Asp Arg Gly Gly Arg Asp
 Trp Tyr Phe Asp Val;
 Asp Gly Phe Leu Arg Asp
 Trp Tyr Phe Asp Val; and
 Ser Gly Tyr Tyr Gly Ser
 Phe Val Gly Phe Ala Tyr .

2. An immunoglobulin H chain variable region fragment having the following amino acid sequence

Glu Val Gln Leu Gln Gln Ser Gly Thr Val
 Leu Ala Arg Pro Gly Ala Ser Val Lys Met
 Ser Cys Lys Ala Ser Gly Tyr Thr Phe Asn
 Ser Tyr Trp Met His Trp Val Lys Gln Arg
 Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala
 Ile Tyr Pro Gly Asn Ser Asp Ile Ser Tyr
 Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu
 Thr Ala Val Thr Ser Thr Ser Thr Ala Tyr
 Met Glu Leu Arg Ser Leu Thr Asn Glu Asp
 Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu
 Tyr Asp Tyr Asp Thr Leu Asp Tyr Trp Gly
 Gln Gly Thr Ser Val Thr Val Ser Ser .

3. An immunoglobulin H chain variable region fragment having the following amino acid sequence

5 Glu Val Lys Leu Val Glu Ser Gly Gly Gly
 Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
 Ser Cys Ala Thr Ser Gly Phe Thr Phe Thr
 Asp Tyr Tyr Met Asn Trp Val Arg Gln Pro
 10 Pro Gly Lys Ala Leu Glu Trp Leu Gly Phe
 Ile Arg Asn Lys Ala Asn Tyr Tyr Thr Thr
 Glu Tyr Ser Ala Ser Val Lys Gly Arg Phe
 Thr Ile Ser Arg Asp Asn Ser Gln Ser Ile
 15 Leu Tyr Leu Gln Met Asn Thr Leu Arg Ala
 Glu Asp Ser Ala Thr Tyr Tyr Cys Ala Arg
 Asp Gly Phe Leu Arg Asp Trp Tyr Phe Asp
 20 Val Trp Gly Ala Gly Thr Thr Val Thr Val
 Ser Ser.

25 4. An immunoglobulin H chain variable region fragment having the following amino acid sequence

30 Glu Val Lys Leu Val Glu Ser Gly Gly Gly
 Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
 Ser Cys Ala Thr Ser Gly Leu Thr Phe Thr
 Asp Tyr Tyr Met Asn Trp Val Arg Gln Pro
 Pro Gly Lys Glu Leu Glu Trp Leu Gly Phe
 35 Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr
 Asp Tyr Ser Ala Ser Val Lys Gly Arg Phe
 Thr Ile Ser Arg Asp Asn Pro Gln Ser Ile
 Leu Tyr Leu Gln Met Asn Thr Leu Thr Thr
 40 Glu Asp Ser Ala Thr Tyr Tyr Cys Ala Arg
 Asp Arg Gly Gly Arg Asp Trp Tyr Phe Asp
 Val Trp Gly Ala Gly Thr Thr Val Thr Val
 45 Ser Ser.

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5. An immunoglobulin H chain variable region fragment having the following amino acid sequence

5 Glu Val Gln Leu Gln Gln Ser Gly Ala Glu
 Leu Ala Arg Pro Gly Ala Ser Val Asn Leu
 Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr
 Asn Tyr Trp Met Gln Trp Val Lys Gln Arg
 10 Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala
 Ile Tyr Pro Gly Asp Gly Asp Thr Arg Tyr
 Thr Gln Lys Phe Lys Gly Lys Ala Thr Leu
 Thr Ala Ala Lys Ser Ser Ser Thr Ala Tyr
 15 Met Gln Leu Ser Ser Leu Ala Ser Glu Asp
 Ser Ala Val Tyr Tyr Cys Ala Arg Ser Gly
 Tyr Tyr Gly Ser Phe Val Gly Phe Ala Tyr
 Trp Gly Gln Gly Thr Leu Val Thr Val Ser
 20 Ala .

- 25 6. DNA and RNA fragments each encoding an immunoglobulin H chain variable region fragment which contains a base sequence encoding a hypervariable region CDR1 having an amino acid sequence selected from

(1) Ser Tyr Trp Met His;
 30 Asp Tyr Tyr Met Asn; and
 Asn Tyr Trp Met Gln ,

a base sequence encoding a hypervariable region CDR2 having an amino acid sequence selected from

35 (2) Ala Ile Tyr Pro Gly Asn Ser
 Asp Ile Ser Tyr Ser Gln Asn
 Phe Lys Asp;
 40 Phe Ile Arg Asn Lys Ala
 Asn Leu Tyr Thr Thr Asp
 Tyr Ser Ala Ser Val Lys
 45 Gly;
 Phe Ile Arg Asn Lys Ala
 Asn Tyr Tyr Thr Thr Glu
 50 Tyr Ser Ala Ser Val Lys
 Gly; and
 Ala Ile Tyr Pro Gly Asp
 Gly Asp Thr Arg Tyr Thr
 55 Glu Lys Phe Lys Gly ,

a base sequence encoding a hypervariable region CDR3 having an amino acid sequence selected from

(3) Glu Glu Tyr Asp Tyr Asp
 5 Thr Leu Asp Tyr;
 Asp Arg Gly Gly Arg Asp
 Trp Tyr Phe Asp Val;
 10 Asp Gly Phe Leu Arg Asp
 Trp Tyr Phe Asp Val; and
 Ser Gly Tyr Tyr Gly Ser
 Phe Val Gly Phe Ala Tyr .
 15

7. An immunoglobulin H chain variable region fragment having following base sequence

20 GAG GTT CAG CTC CAG CAG TCT GGG ACT GTG
 CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG
 TCC TGC AAG GCT TCG GGC TAC ACC TTT AAC
 25 AGC TAC TGG ATG CAC TGG GTA AAA CAG AGG
 CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG
 ATT TAT CCT GGA AAT AGT GAT ATT AGC TAC
 30 AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG
 ACT GCC GTC ACA TCC ACC AGC ACT GCC TAC
 ATG GAA CTC AGA AGC CTG ACA AAT GAG GAC
 TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA
 35 TAT GAT TAC GAC ACC CTG GAC TAC TGG GGT
 CAA GGA ACC TCA GTC ACC GTC TCC TCA.
 40
 45
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8. An immunoglobulin H chain variable region fragment having the following base sequence

5 GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC
 TTG GTA CAG CCT GGG GGT TCT CTC AGA CTC
 TCC TGT GCA ACT TCT GGG TTA ACC TTC ACT
 GAT TAC TAC ATG AAC TGG GTC CGC CAG CCT
 10 CCA GGA AAG GAA CTT GAA TGG TTG GGT TTT
 ATT AGA AAC AAA GCT AAT CTT TAC ACA ACA
 GAC TAC AGT GCA TCT GTG AAG GGT CGG TTC
 ACC ATC TCC AGA GAT AAT CCC CAA AGC ATC
 15 CTC TAT CTT CAA ATG AAC ACC CTG ACA ACT
 GAG GAC AGT GCC ACT TAT TAC TGT GCA AGA
 GAT AGG GGG GGG AGG GAC TGG TAC TTC GAT
 GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC
 20 TCC TCA .

- 25 9. An immunoglobulin H chain variable region fragment having the following base sequence

30 GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC
 TTG GTA CAG CCT GGG GGT TCT CTG AGA CTC
 TCC TGT GCA ACT TCT GGG TTC ACC TTC ACT
 GAT TAC TAC ATG AAC TGG GTC CGC CAG CCT
 CCA GGA AAG GCA CTT GAG TGG TTG GGT TTT
 35 ATT AGA AAC AAA GCT AAT TAT TAC ACA ACA
 GAG TAC AGT GCA TCT GTG AAG GGT CGG TTC
 ACC ATC TCC AGA GAT AAT TCC CAA AGC ATC
 CTC TAT CTT CAA ATG AAC ACC CTG AGA GCT
 40 GAG GAC AGT GCC ACT TAT TAC TGT GCA AGA
 GAT GGG TTC CTA CGG GAC TGG TAC TTC GAT
 GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC
 45 TCC TCA .

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10. An immunoglobulin H chain variable region fragment having the following base sequence

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5      GAG GTT CAG CTC CAG CAG TCT GGG GCT GAA
      CTG GCA AGA CCT GGG GCT TCA GTG AAC TTG
      TCC TGC AAG GCT TCT GGC TAC ACC TTT ACT
      AAC TAC TGG ATG CAG TGG GTA AAA CAG AGG
10     CCT GGA CAG GGT CTG GAA TGG ATT GGG GCT
      ATT TAT CCT GGA GAT GGT GAT ACT AGG TAC
      ACT CAG AAG TTC AAG GGC AAG GCC ACA TTG
      ACT GCA GCT AAA TCC TCC AGC ACA GCC TAC
15     ATG CAA CTC AGC AGC TTG GCA TCT GAG GAC
      TCT GCG GTC TAT TAC TGT GCA AGA TCG GGC
      TAC TAT GGT AGC TTC GTT GGG TTT GCT TAC
      TGG GGC CAA GGG ACT CTG GTC ACT GTC TCT
20     GCA .

```

25 11. An immunoglobulin L chain variable region fragment which contains a hypervariable region CDR1 having an amino acid sequence selected from

```

30     (1) Tyr Arg Ala Ser Lys Ser Val
      Gln Leu His Leu Ala Ile Val
      Tyr Met His;
      Tyr Arg Ala Ser Lys Ser Val
      Ser Thr Ser Gly Tyr Ser Tyr
35     Met His;
      Lys Ala Ser Gln Asp Val Asn
      Thr Ala Val Ala; and
      Lys Ala Ser Gln Asp Val Thr
40     Thr Asp Val Ala ,

```

a hypervariable region CDR2 having an amino acid sequence selected from

```

45     (2) Leu Val Ser Asn Leu Glu Ser;
      Leu Val Ser Asn Leu Asp Ser; and
      Ser Ala Ser Tyr Arg Tyr Thr,
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and a hypervariable region CDH3 having an amino acid sequence selected from

(3) Gln His Ile Arg Val Ala Tyr
 Thr;
 Gln His Ile Arg Gly Ala Tyr
 Thr;
 Gln His Ile Glu Gly Ala Tyr
 Thr;
 Gln Gln His Tyr Ser Pro Pro
 Leu Thr; and
 Gln Gln His Tyr Ser Thr Ala
 Trp Thr .

12. An immunoglobulin L chain variable region fragment having the following amino acid sequence

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser
 Leu Ala Val Ser Pro Leu Gly Gln Arg Ala
 Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val
 Gln Leu His Leu Ala Ile Val Tyr Met His
 Trp Asn Gln Gln Lys Pro Gly Gln Pro Pro
 Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu
 Glu Ser Gly Val Pro Ala Arg Phe Ser Gly
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn
 Ile His Pro Val Glu Glu Glu Asp Ala Ala
 Thr Tyr Tyr Cys Gln His Ile Arg Val Ala
 Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu
 Ile Lys .

13. An immunoglobulin L chain variable region fragment having the following amino acid sequence

5 Asp Ile Val Leu Thr Gln Ser Pro Ala Ser
 Leu Ala Val Ser Leu Gly Gln Arg Ala Ser
 Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser
 Thr Ser Gly Tyr Ser Tyr Met His Trp Asn
 10 Gln Gln Lys Pro Gly Gln Pro Pro Arg Leu
 Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
 Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 15 Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr
 Tyr Cys Gln His Ile Arg Gly Ala Tyr Thr
 Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys.

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14. An immunoglobulin L chain variable region fragment having the following amino acid sequence

25 Asp Ile Val Leu Thr Gln Ser Pro Ala Ser
 Leu Ala Val Ser Leu Gly Gln Arg Ala Thr
 Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser
 Thr Ser Gly Tyr Ser Tyr Met His Trp Asn
 30 Gln Gln Arg Pro Gly Gln Pro Pro Arg Leu
 Leu Ile Tyr Leu Val Ser Asn Leu Asp Ser
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
 35 Ser Gly Thr Asp Phe Thr Leu Asn Ile His
 Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr
 Tyr Cys Gln His Ile Glu Gly Ala Tyr Thr
 40 Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys.

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15. An immunoglobulin L chain variable region fragment having the following amino acid sequence

Asp Ile Val Met Thr Gln Ser His Lys Phe
 Met Ser Thr Ser Val Gly Asp Arg Val Ser
 Ile Thr Cys Lys Ala Ser Gln Asp Val Asn
 Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro
 Gly Gln Ser Pro Lys Leu Leu Leu Tyr Ser
 Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp
 His Phe Thr Gly Ser Gly Ser Gly Thr Asp
 Phe Thr Phe Thr Ile Ser Gly Val Gln Ala
 Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln
 His Tyr Ser Pro Pro Leu Thr Phe Gly Ala
 Gly Thr Lys Leu Glu Leu Lys .

16. An immunoglobulin L chain variable region fragment having the following amino acid sequence

Asp Ile Val Met Thr Gln Ser His Lys Phe
 Met Ser Thr Ser Val Gly Asp Arg Val Thr
 Ile Thr Cys Lys Ala Ser Gln Asp Val Thr
 Thr Asp Val Ala Trp Tyr Gln Gln Lys Pro
 Arg Gln Ser Pro Lys Leu Leu Ile Tyr Ser
 Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp
 Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp
 Phe Thr Phe Thr Ile Ser Ser Val Gln Ala
 Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln
 His Tyr Ser Thr Ala Trp Thr Phe Gly Gly
 Gly Thr Lys Leu Glu Ile Lys .

17. DNA and RNA fragments each encoding an immunoglobulin L chain variable region fragment which contains a base sequence encoding a hypervariable region CDR1 having an amino acid sequence selected from

5 (1) Tyr Arg Ala Ser Lys Ser Val
Gln Leu His Leu Ala Ile Val
Tyr Met His;
Tyr Arg Ala Ser Lys Ser Val
10 Ser Thr Ser Gly Tyr Ser Tyr
Met His;
Lys Ala Ser Gln Asp Val Asn
Thr Ala Val Ala; and
15 Lys Ala Ser Gln Asp Val Thr
Thr Asp Val Ala ,

20 a base sequence encoding a hypervariable region CDR2 having an amino acid sequence selected from

(2) Leu Val Ser Asn Leu Glu Ser;
Leu Val Ser Asn Leu Asp Ser; and
25 Ser Ala Ser Tyr Arg Tyr Thr ,

and a base sequence encoding a hypervariable region CDR3 having an amino acid sequence selected from

30 (3) Gln His Ile Arg Val Ala Tyr
Thr;
Gln His Ile Arg Gly Ala Tyr
35 Thr;
Gln His Ile Glu Gly Ala Tyr
Thr;
Gln Gln His Tyr Ser Pro Pro
40 Leu Thr; and
Gln Gln His Tyr Ser Thr Ala
Trp Thr .

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18. An immunoglobulin L chain variable region fragment having the following base sequence

5 GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC
TTA GCT GTA TCT CCT CTG GGG CAG AGG GCC
ACC ATC TCA TAC AGG GCC AGC AAA AGT GTG
CAG TTA CAT CTG GCT ATA GTT TAT ATG CAC
10 TGG AAC CAA CAG AAA CCA GGA CAG CCA CCC
AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA
GAA TCT GGG GTC CCT GCC AGG TTC AGT GGC
AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC
15 ATC CAT CCT GTG GAG GAG GAG GAT GCT GCA
ACC TAT TAC TGT CAG CAC ATT AGG GTA GCT
TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA
20 ATA AAA .

19. An immunoglobulin L chain variable region fragment having the following base sequence

25 GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC
TTA GCT GTA TCT CTG GGG CAG AGG GCC TCC
ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT
30 ACA TCT GGC TAT AGT TAT ATG CAC TGG AAC
CAA CAG AAA CCA GGA CAG CCA CCC AGA CTC
CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT
35 GGG GTC CCT GCC AGG TTC AGT GGC AGT GGG
TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT
CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT
40 TAC TGT CAG CAC ATT AGG GGA GCT TAC ACG
TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA .

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20. An immunoglobulin L chain variable region fragment having the following base sequence

```

5      GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC
      TTA GCT GTA TCT CTG GGG CAG AGG GCC ACC
      ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT
      ACA TCT GGC TAT AGT TAT ATG CAC TGG AAC
      CAA CAG AGA CCA GGA CAG CCA CCC AGA CTC
10     CTC ATC TAT CTT GTA TCC AAC CTA GAC TCT
      GGG GTC CCT GCC AGG TTC AGT GGC AGT GGG
      TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT
      CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT
15     TAC TGT CAG CAC ATT GAG GGA GCT TAC ACG
      TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA .

```

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21. An immunoglobulin L chain variable region fragment having the following base sequence

```

25     GAC ATT GTG ATG ACC CAG TCT CAC AAA TTC
      ATG TCC ACA TCA GTA GGA GAC AGG GTC AGT
      ATC ACC TGC AAG GCC AGT CAG GAT GTG AAT
      ACT GCT GTA GCC TGG TAT CAA CAG AAA CCA
30     GGA CAA TCT CCT AAA CTA CTG CTT TAC TCG
      GCA TCC TAC CGG TAC ACT GGA GTC CCT GAT
      CAC TTC ACT GGC AGT GGA TCT GGG ACG GAT
      TTC ACT TTC ACC ATC AGC GGT GTG CAG GCT
35     GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA
      CAT TAT AGT CCT CCT CTC ACG TTC GGT GCT
      GGG ACC AAG CTG GAA CTG AAA .
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22. An immunoglobulin L chain variable region fragment having the following base sequence

5 GAC ATT GTG ATG ACA CAG TCT CAC AAA TTC
 ATG TCC ACA TCA GTT GGA GAC AGG GTC ACC
 ATC ACC TGC AAG GCC AGT CAG GAT GTG ACT
 ACT GAT GTA GCC TGG TAT CAA CAG AAA CCA
 10 CGA CAA TCT CCT AAA CTA CTG ATT TAC TCG
 GCA TCC TAT CGG TAC ACT GGA GTC CCT GAT
 CGC TTC ACT GGC AGT GGA TCT GGG ACG GAT
 TTC ACT TTC ACC ATC AGC AGT GTG CAG GCT
 15 GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA
 CAT TAT AGT ACT GCG TGG ACG TTC GGT GGT
 GGC ACC AAG CTG GAA ATC AAA .

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23. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 2 and the immunoglobulin L chain variable region fragment according to claim 12.

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24. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 2 and the immunoglobulin L chain variable region fragment according to claim 13.

25. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 3 and the immunoglobulin L chain variable region fragment according to claim 14.

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26. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 4 and the immunoglobulin L chain variable region fragment according to claim 15.

27. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 5 and the immunoglobulin L chain variable region fragment according to claim 16.

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FIG. 1

Idio 3

Idio 17

Idio 20

Idio 27

Idio 33

+	λ	K	G3	G2b	G2a	G1	M	A
+	λ	K	G3	G2b	G2a	G1	M	A
+	λ	K	G3	G2b	G2a	G1	M	A
+	λ	K	G3	G2b	G2a	G1	M	A
+	λ	K	G3	G2b	G2a	G1	M	A

FIG. 2

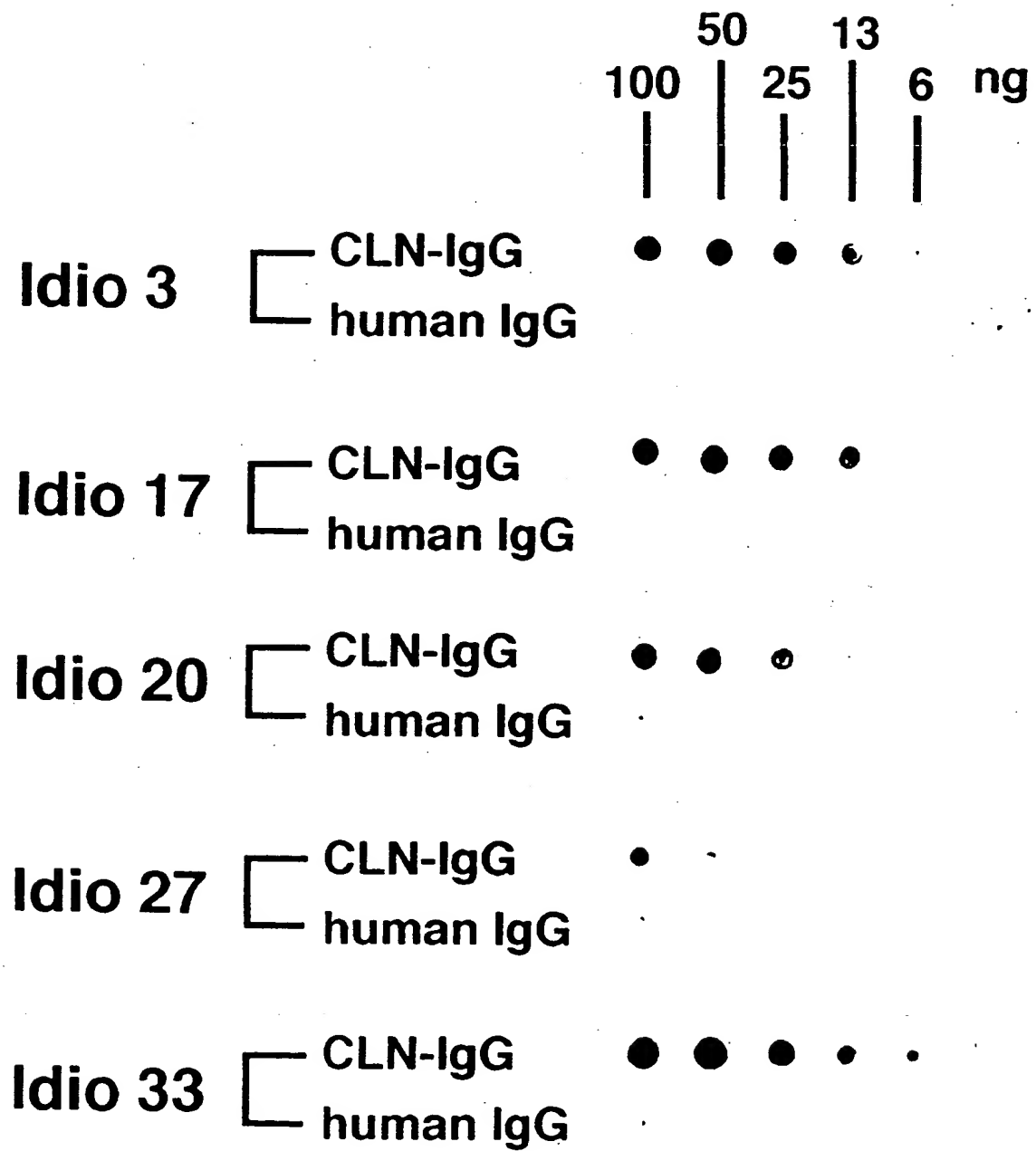


FIG. 3

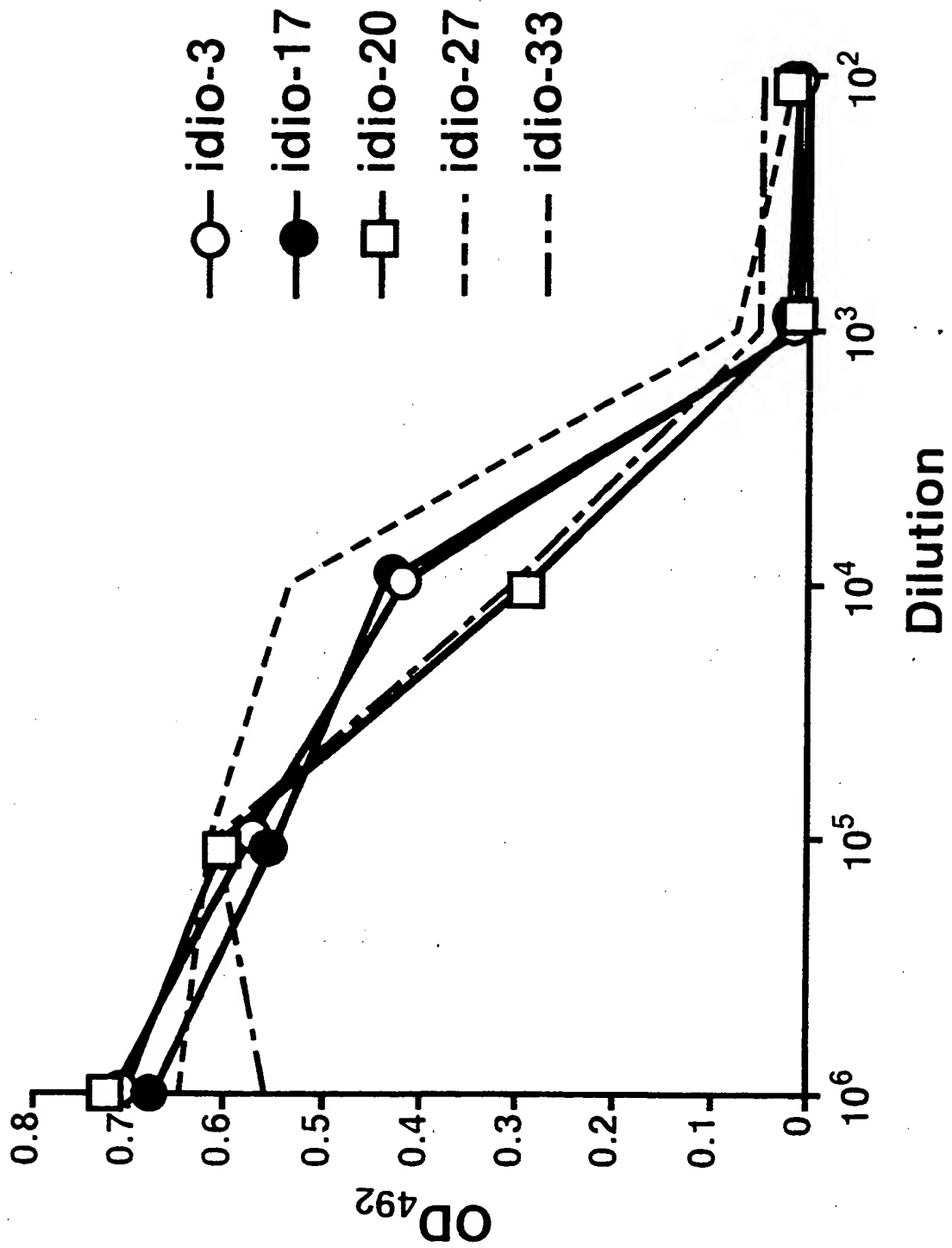


FIG. 4

3 17 20 27 33

FR 1	1	Glu	Glu	Glu	Glu	Glu
	2	Val	Val	Val	Val	Val
	3	Gln	Gln	Lys	Lys	Gln
	4	Leu	Leu	Leu	Leu	Leu
	5	Gln	Gln	Val	Val	Gln
	6	Gln	Gln	Glu	Glu	Gln
	7	Ser	Ser	Ser	Ser	Ser
	8	Gly	Gly	Gly	Gly	Gly
	9	Thr	Thr	Gly	Gly	Ala
	10	Val	Val	Gly	Gly	Glu
	11	Leu	Leu	Leu	Leu	Leu
	12	Ala	Ala	Val	Val	Ala
	13	Arg	Arg	Gln	Gln	Arg
	14	Pro	Pro	Pro	Pro	Pro
	15	Gly	Gly	Gly	Gly	Gly
	16	Ala	Ala	Gly	Gly	Ala
	17	Ser	Ser	Ser	Ser	Ser
	18	Val	Val	Leu	Leu	Val
	19	Lys	Lys	Arg	Arg	Asn
	20	Met	Met	Leu	Leu	Leu
	21	Ser	Ser	Ser	Ser	Ser
	22	Cys	Cys	Cys	Cys	Cys
	23	Lys	Lys	Ala	Ala	Lys
	24	Ala	Ala	Thr	Thr	Ala
	25	Ser	Ser	Ser	Ser	Ser
	26	Gly	Gly	Gly	Gly	Gly
	27	Tyr	Tyr	Leu	Phe	Tyr
	28	Thr	Thr	Thr	Thr	Thr
	29	Phe	Phe	Phe	Phe	Phe
	30	Asn	Asn	Thr	Thr	Thr
CDR 1	31	Ser	Ser	Asp	Asp	Asn
	32	Tyr	Tyr	Tyr	Tyr	Tyr
	33	Trp	Trp	Tyr	Tyr	Trp
	34	Met	Met	Met	Met	Met
FR 2	35	His	His	Asn	Asn	Gln
	36	Trp	Trp	Trp	Trp	Trp
	37	Val	Val	Val	Val	Val
	38	Lys	Lys	Arg	Arg	Lys
	39	Gln	Gln	Gln	Gln	Gln
	40	Arg	Arg	Pro	Pro	Arg
	41	Pro	Pro	Pro	Pro	Pro
	42	Gly	Gly	Gly	Gly	Gly
	43	Gln	Gln	Lys	Lys	Gln
	44	Gly	Gly	Glu	Ala	Gly
	45	Leu	Leu	Leu	Leu	Leu
	46	Glu	Glu	Glu	Glu	Glu
	47	Trp	Trp	Trp	Trp	Trp
	48	Ile	Ile	Leu	Leu	Ile
	49	Gly	Gly	Gly	Gly	Gly
CDR 2	50	Ala	Ala	Phe	Phe	Ala
	51	Ile	Ile	Ile	Ile	Ile
	52	Tyr	Tyr	Arg	Arg	Tyr
	52A	Pro	Pro	Asn	Asn	Pro
	52B	---	---	Lys	Lys	---
	52C	---	---	Ala	Ala	---
	53	Gly	Gly	Asn	Asn	Gly
	54	Asn	Asn	Leu	Tyr	Asp
	55	Ser	Ser	Tyr	Tyr	Gly
	56	Asp	Asp	Thr	Thr	Asp
	57	Ile	Ile	Thr	Thr	Thr
	58	Ser	Ser	Asp	Glu	Arg
	59	Tyr	Tyr	Tyr	Tyr	Tyr
	60	Ser	Ser	Ser	Ser	Thr
	61	Gln	Gln	Ala	Ala	Gln
	62	Asn	Asn	Ser	Ser	Lys
	63	Phe	Phe	Val	Val	Phe
	64	Lys	Lys	Lys	Lys	Lys
	65	Asp	Asp	Gly	Gly	Gly
	66	Arg	Arg	Arg	Arg	Lys
	67	Ala	Ala	Phe	Phe	Ala

FR 3	68	Lys	Lys	Thr	Thr	Thr
	69	Leu	Leu	Ile	Ile	Leu
	70	Thr	Thr	Ser	Ser	Thr
	71	Ala	Ala	Arg	Arg	Ala
	72	Val	Val	Asp	Asp	Ala
	73	Thr	Thr	Asn	Asn	Lys
	74	Ser	Ser	Pro	Ser	Ser
	75	Thr	Thr	Gln	Gln	Ser
	76	Ser	Ser	Ser	Ser	Ser
	77	Thr	Thr	Ile	Ile	Thr
	78	Ala	Ala	Leu	Leu	Ala
	79	Tyr	Tyr	Tyr	Tyr	Tyr
	80	Met	Met	Leu	Leu	Met
	81	Glu	Glu	Gln	Gln	Gln
	82	Leu	Leu	Met	Met	Leu
	82A	Arg	Arg	Asn	Asn	Ser
	82B	Ser	Ser	Thr	Thr	Ser
	82C	Leu	Leu	Leu	Leu	Leu
	83	Thr	Thr	Thr	Arg	Ala
	84	Asn	Asn	Thr	Ala	Ser
	85	Glu	Glu	Glu	Glu	Glu
	86	Asp	Asp	Asp	Asp	Asp
	87	Ser	Ser	Ser	Ser	Ser
	88	Ala	Ala	Ala	Ala	Ala
	89	Val	Val	Thr	Thr	Val
	90	Tyr	Tyr	Tyr	Tyr	Tyr
	91	Phe	Phe	Tyr	Tyr	Tyr
	92	Cys	Cys	Cys	Cys	Cys
	93	Thr	Thr	Ala	Ala	Ala
	94	Lys	Lys	Arg	Arg	Arg
CDR 3	95	Glu	Glu	Asp	Asp	Ser
	96	Glu	Glu	Arg	Gly	Gly
	97	Tyr	Tyr	Gly	Phe	Tyr
	98	Asp	Asp	Gly	Leu	Tyr
	99	Tyr	Tyr	Arg	Arg	Gly
	100	Asp	Asp	Asp	Asp	Ser
	100A	Thr	Thr	---	---	Phe
	100B	---	---	---	---	Val
	100C	---	---	---	---	Gly
	100D	---	---	---	---	---
FR 4	100E	---	---	---	---	---
	100F	---	---	---	---	---
	100G	---	---	---	---	---
	100H	---	---	---	---	---
	100I	---	---	Trp	Trp	---
	100J	---	---	Tyr	Tyr	---
	100K	Leu	Leu	Phe	Phe	Phe
	101	Asp	Asp	Asp	Asp	Ala
	102	Tyr	Tyr	Val	Val	Tyr
	103	Trp	Trp	Trp	Trp	Trp
	104	Gly	Gly	Gly	Gly	Gly
	105	Gln	Gln	Ala	Ala	Gln
	106	Gly	Gly	Gly	Gly	Gly
	107	Thr	Thr	Thr	Thr	Thr
	108	Ser	Ser	Thr	Thr	Leu
	109	Val	Val	Val	Val	Val
	110	Thr	Thr	Thr	Thr	Thr
	111	Val	Val	Val	Val	Val
	112	Ser	Ser	Ser	Ser	Ser
	113	Ser	Ser	Ser	Ser	Ala

FIG. 5

3 17 20 27 33

F R 1	1	Asp	Asp	Asp	Asp	Asp
	2	Ile	Ile	Ile	Ile	Ile
	3	Val	Val	Val	Val	Val
	4	Leu	Leu	Leu	Met	Met
	5	Thr	Thr	Thr	Thr	Thr
	6	Gln	Gln	Gln	Gln	Gln
	7	Ser	Ser	Ser	Ser	Ser
	8	Pro	Pro	Pro	His	His
	9	Ala	Ala	Ala	Lys	Lys
	10	Ser	Ser	Ser	Phe	Phe
	11	Leu	Leu	Leu	Met	Met
	12	Ala	Ala	Ala	Ser	Ser
	13	Val	Val	Val	Thr	Thr
	14	Ser	Ser	Ser	Ser	Ser
	15	Pro	Leu	Leu	Val	Val
	16	Leu	Gly	Gly	Gly	Gly
	17	Gly	Gln	Gln	Asp	Asp
	18	Gln	Arg	Arg	Arg	Arg
	19	Arg	Ala	Ala	Val	Val
	20	Ala	Ser	Thr	Ser	Thr
	21	Thr	Ile	Ile	Ile	Ile
	22	Ile	Ser	Ser	Thr	Thr
	23	Ser	---	---	Cys	Cys
C D R 1	24	Tyr	Tyr	Tyr	Lys	Lys
	25	Arg	Arg	Arg	Ala	Ala
	26	Ala	Ala	Ala	Ser	Ser
	27	Ser	Ser	Ser	Gln	Gln
	27A	Lys	Lys	Lys	---	---
	27B	Ser	Ser	Ser	---	---
	27C	Val	Val	Val	---	---
	27D	Gln	Ser	Ser	---	---
	27E	Leu	Thr	Thr	---	---
	27F	His	---	---	---	---
	28	Leu	Ser	Ser	Asp	Asp
	29	Ala	Gly	Gly	Val	Val
F R 2	30	Ile	Tyr	Tyr	Asn	Thr
	31	Val	Ser	Ser	Thr	Thr
	32	Tyr	Tyr	Tyr	Ala	Asp
	33	Met	Met	Met	Val	Val
	34	His	His	His	Ala	Ala
	35	Trp	Trp	Trp	Trp	Trp
	36	Asn	Asn	Asn	Tyr	Tyr
	37	Gln	Gln	Gln	Gln	Gln
	38	Gln	Gln	Gln	Gln	Gln
	39	Lys	Lys	Arg	Lys	Lys
	40	Pro	Pro	Pro	Pro	Pro
	41	Gly	Gly	Gly	Gly	Arg
C D R 2	42	Gln	Gln	Gln	Gln	Gln
	43	Pro	Pro	Pro	Ser	Ser
	44	Pro	Pro	Pro	Pro	Pro
	45	Arg	Arg	Arg	Lys	Lys
	46	Leu	Leu	Leu	Leu	Leu
	47	Leu	Leu	Leu	Leu	Leu
	48	Ile	Ile	Ile	Leu	Ile
	49	Tyr	Tyr	Tyr	Tyr	Tyr
	50	Leu	Leu	Leu	Ser	Ser
	51	Val	Val	Val	Ala	Ala
	52	Ser	Ser	Ser	Ser	Ser
	53	Asn	Asn	Asn	Tyr	Tyr
F R 3	54	Leu	Leu	Leu	Arg	Arg
	55	Glu	Glu	Asp	Tyr	Tyr
	56	Ser	Ser	Ser	Thr	Thr
	57	Gly	Gly	Gly	Gly	Gly
	58	Val	Val	Val	Val	Val
	59	Pro	Pro	Pro	Pro	Pro
	60	Ala	Ala	Ala	Asp	Asp
	61	Arg	Arg	Arg	His	Arg
	62	Phe	Phe	Phe	Phe	Phe
	63	Ser	Ser	Ser	Thr	Thr
	64	Gly	Gly	Gly	Gly	Gly
	65	Ser	Ser	Ser	Ser	Ser
C D R 3	66	Gly	Gly	Gly	Gly	Gly
	67	Gly	Ser	Ser	Ser	Ser
	68	Gly	Gly	Gly	Gly	Gly
	69	Thr	Thr	Thr	Thr	Thr
	70	Asp	Asp	Asp	Asp	Asp
	71	Phe	Phe	Phe	Phe	Phe
	72	Thr	Thr	Thr	Thr	Thr
	73	Leu	Leu	Leu	Phe	Phe
	74	Asn	Asn	Asn	Thr	Thr
	75	Ile	Ile	Ile	Ile	Ile
	76	His	His	His	Ser	Ser
	77	Pro	Pro	Pro	Ser	Ser
F R 4	78	Val	Val	Val	Val	Val
	79	Glu	Glu	Glu	Gln	Gln
	80	Glu	Glu	Glu	Ala	Ala
	81	Glu	Glu	Glu	Glu	Glu
	82	Asp	Asp	Asp	Asp	Asp
	83	Ala	Ala	Ala	Leu	Leu
	84	Ala	Ala	Ala	Ala	Ala
	85	Thr	Thr	Thr	Val	Val
	86	Tyr	Tyr	Tyr	Tyr	Tyr
	87	Tyr	Tyr	Tyr	Tyr	Tyr
	88	Cys	Cys	Cys	Cys	Cys
	89	Gln	Gln	Gln	Gln	Gln
F R 5	90	His	His	His	Gln	Gln
	91	Ile	Ile	Ile	His	His
	92	Arg	Arg	Glu	Tyr	Tyr
	93	Val	Gly	Gly	Ser	Ser
	94	Ala	Ala	Ala	Pro	Thr
	95	---	---	---	Pro	Ala
	95A	---	---	---	---	---
	95B	---	---	---	---	---
	95C	---	---	---	---	---
	95D	---	---	---	---	---
	95E	---	---	---	---	---
	95F	---	---	---	---	---
F R 6	96	Tyr	Tyr	Tyr	Leu	Trp
	97	Thr	Thr	Thr	Thr	Thr
	98	Phe	Phe	Phe	Phe	Phe
	99	Gly	Gly	Gly	Gly	Gly
	100	Gly	Gly	Gly	Ala	Gly
	101	Gly	Gly	Gly	Gly	Gly
	102	Thr	Thr	Thr	Thr	Thr
	103	Lys	Lys	Lys	Lys	Lys
	104	Leu	Leu	Leu	Leu	Leu
	105	Glu	Glu	Glu	Glu	Glu
	106	Ile	Ile	Ile	Leu	Ile
	106A	---	---	---	---	---
	107	Lys	Lys	Lys	Lys	Lys



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EUROPEAN SEARCH REPORT

Application Number
EP 94 11 5683

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. CL. 6)
A	US-A-5 208 146 (R. ERIE) * the whole document * ---	1-27	C12N15/13 C07K16/42
A	WO-A-89 00050 (AKZO NV) * claims * * examples * ---	1-27	
A	WO-A-93 10221 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) * the whole document * ---	1-27	
A	EUROPEAN JOURNAL OF CANCER AND CLINICAL ONCOLOGY, vol.24, no.5, May 1988, OXFORD, GB pages 829 - 838 Y. AOTSUKA ET AL. 'Identification of a malignant cell associated antigen recognized by a human monoclonal antibody.' * abstract * ---	1-27	
A	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE USA, vol.80, no.20, October 1983, WASHINGTON DC, USA pages 6327 - 6331 M. GLASSY ET AL. 'UC 729-6, a human lymphoblastoid B-cell line useful for generating antibody-secreting human-human hybridomas.' * abstract * --- -/--	1-27	TECHNICAL FIELDS SEARCHED (Int. CL. 6) C12N C07K
The present search report has been drawn up for all claims			
Place of search THE HAGUE		Date of completion of the search 16 March 1995	Examiner Nooij, F
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document</p>			

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EUROPEAN SEARCH REPORT

Application Number
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A	CANCER RESEARCH, vol.52, no.9, 1 May 1992, PHILADELPHIA PA, USA pages 2603 - 2609 W. TADDEI-PETERS ET AL. 'Quantitation of human tumor-reactive monoclonal antibody 16.88 in the circulation and localization of 16.88 in colorectal metastatic tumor tissue using murine antiidiotypic antibodies.' * abstract *	1-27	
P,A	MOLECULAR IMMUNOLOGY, vol.30, no.16, November 1993, OXFORD, GB pages 1481 - 1489 K. YAGO ET AL. 'Immunoglobulin variable region sequences of two human monoclonal antibodies directed to an onco-developmental carbohydrate antigen, lactotetraosylceramide (LcOse4Cer).' * abstract *	1-27	
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Place of search THE HAGUE		Date of completion of the search 16 March 1995	Examiner Nooij, F
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